Ritalin revisited: does it really help in neurological injury?
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Methylphenidate (Ritalin) is a commonly used central nervous stimulant. It has been used in various neurological conditions, including attention deficit disorder, depression, and narcolepsy. Methylphenidate has been advocated in patients with traumatic brain injury and stroke for a variety of cognitive, attention, and behavioral problems. It also has been shown to speed recovery from poststroke depression so that patients can participate more fully in rehabilitation programs. Research suggests that it also may have a role in augmenting activity of injured neuronal tissue in the comatose patient, thus facilitating a return to consciousness. The neuroscience nurse plays an important role in monitoring response to Ritalin, including identifying its side effects. A review of the limited studies on the use of Ritalin, its mechanisms of action, dosing, and weaning provide a current understanding of this adjunctive agent's role in treatment for the neurological population.

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Clinical Research Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Boston, Massachusetts. Harvard Medical School, Boston, Massachusetts.

OBJECTIVE: Concerns exist that stimulant therapy of youths with attention-deficit/hyperactivity disorder (ADHD) may result in an increased risk for subsequent substance use disorders (SUD). We investigated all long-term studies in which pharmacologically treated and untreated youths with ADHD were examined for later SUD outcomes. METHODS: A search of all available prospective and retrospective studies of children, adolescents, and adults with ADHD that had information relating childhood exposure to stimulant therapy and later SUD outcome in adolescence or adulthood was conducted through PubMed supplemented with data from scientific presentations. Meta-analysis was used to evaluate the relationship between stimulant therapy and subsequent SUD in youths with ADHD in general while addressing specifically differential effects on alcohol use disorders or drug use disorders and the potential effects of covariates. RESULTS: Six studies-2 with follow-up in adolescence and 4 in young adulthood- were included and comprised 674 medicated subjects and 360 unmedicated subjects who were followed at least 4 years. The pooled estimate of the odds ratio indicated a 1.9-fold reduction in risk for SUD in youths who were treated with stimulants compared with youths who
did not receive pharmacotherapy for ADHD ($z = 2.1$; 95% confidence interval for odds ratio [OR]: 1.1-3.6). We found similar reductions in risk for later drug and alcohol use disorders ($z = 1.1$). Studies that reported follow-up into adolescence showed a greater protective effect on the development of SUD (OR: 5.8) than studies that followed subjects into adulthood (OR: 1.4). Additional analyses showed that the results could not be accounted for by any single study or by publication bias. CONCLUSION: Our results suggest that stimulant therapy in childhood is associated with a reduction in the risk for subsequent drug and alcohol use disorders.

JAMA 2003 Jan 1;289(1):49-55

**Prevalence of Autism in a US Metropolitan Area.**

Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Centers for Disease Control and Prevention (F-15), 4770 Buford Hwy NE, Atlanta, GA 30341. mxy1@cdc.gov

CONTEXT: Concern has been raised about possible increases in the prevalence of autism. However, few population-based studies have been conducted in the United States. OBJECTIVES: To determine the prevalence of autism among children in a major US metropolitan area and to describe characteristics of the study population. DESIGN, SETTING, AND POPULATION: Study of the prevalence of autism among children aged 3 to 10 years in the 5 counties of metropolitan Atlanta, Ga, in 1996. Cases were identified through screening and abstracting records at multiple medical and educational sources, with case status determined by expert review. MAIN OUTCOME MEASURES: Autism prevalence by demographic factors, levels of cognitive functioning, previous autism diagnoses, special education eligibility categories, and sources of identification. RESULTS: A total of 987 children displayed behaviors consistent with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for autistic disorder, pervasive developmental disorder-not otherwise specified, or Asperger disorder. The prevalence for autism was 3.4 per 1000 (95% confidence interval [CI], 3.2-3.6) (male-female ratio, 4:1). Overall, the prevalence was comparable for black and white children (black, 3.4 per 1000 [95% CI, 3.0-3.7] and white, 3.4 per 1000 [95% CI, 3.2-3.7]). Sixty-eight percent of children with IQ or developmental test results ($N = 880$) had cognitive impairment. As severity of cognitive impairment increased from mild to profound, the male-female ratio decreased from 4.4 to 1.3. Forty percent of children with autism were identified only at educational sources. Schools were the most important source for information on black children, children of younger mothers, and children of mothers with less than 12 years of education. CONCLUSION: The rate of autism found in this study was higher than the rates from studies conducted in the United States during the 1980s and early 1990s, but it was consistent with those of more recent studies.


**Outcome research in Asperger syndrome and autism.**
This article presents findings from the outcome literature on autism, Asperger syndrome (AS), and related disorders. The discussion of outcome principally focuses on life adaptation, but also considers outcome in AS in relationship to other diagnostic groups and across time. The current research in this area is neither substantial nor systematic. Thus, in this examination of the literature, the goal is to highlight salient findings, but also to put forward questions that might direct meaningful research in this area for the future and to consider implications for treatment.

Methods 2003 May;30(1):64-78

Independently movable multielectrode array to record multiple fast-spiking neurons in the cerebral cortex during cognition.

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A multiple microelectrode carrier system is described that allows each of 16 microelectrodes in a high-density array to be manipulated in the brain independently by remote control during a cognitive task. Descriptions of the carrier system, advancing techniques, and microelectrode design are presented that allow high-fidelity, extracellular recordings of multiple cerebral cortex neurons with high signal-to-noise ratio and day-to-day repeatability. The motivation for the new carrier system was to provide a method to target multi-microelectrode recordings to a distinct population of fast-spiking neurons in the cerebral cortex during a behavioral task to assess their involvement in selective attention. Recent work using intracellular recording in vitro and single-neuron extracellular recordings in vivo has demonstrated that subpopulations of cortical interneurons can be identified on the basis of their action potential waveform and response to sensory input, and that such interneurons play a fundamental role in generating cortical rhythmicity associated with vigilant wakefulness. A new behavioral paradigm is presented, based on Pavlov’s and Kamin’s classic work on compound conditioning, that permits the electrophysiological patterns of selective attention among neuronal ensembles to be distinguished from those of sensation without attention in a primary sensory cortex. Our approach of multiple, individually guided cerebral cortical recordings in behaving rats during a complex cognitive task is beginning to provide new support for the role of fast cerebral rhythms in selective attention.

(Replication of Thatcher’s several previous studies...)


The effect of a brain injury on the quantitative EEG (QEEG) variables during an auditory memory activation condition was examined with 56 normal subjects and 85 mild traumatic brain-injured (MTBI) subjects. An analysis was conducted on the different response patterns of the two groups, the variables which were correlated with memory performance in the brain-
injured group, and the variables which predicted the memory score for the combined two groups (normal and brain injured). The three conditions included the input task, the immediate recall, and the delayed recall task. The consistent effect of a brain injury was a lowering of the connectivity patterns in the beta1 and beta2 frequencies (phase and coherences) and increases predominantly in the relative power of beta1 (13–32 Hz), which were correlated with the differences in recall. There is a subtle shift to right hemisphere/right temporal functioning and employment of the higher beta1 and beta2 frequencies (phase and coherence) in the response pattern of the MTBI subject. Memory functioning is predominantly positively correlated with connection activity (phase and coherence) and negatively correlated with beta activation at specific locations.

Clin Electroencephalogr 2003 Jan;34(1):1-4
**Predicting outcome in acute stroke: a comparison between QEEG and the Canadian Neurological Scale.**
Cuspineda E, Machado C, Aubert E, Galan L, Llopis F, Avila Y.
Institute of Clinical Neurophysiology, Havana, Cuba.
OBJECTIVE: To determine and compare the predictive value of quantitative EEG (QEEG) and the Canadian Neurological Scale (CaNS), in patients with an acute cerebral stroke.
METHODOLOGY: Twenty-eight patients were studied with the diagnosis of acute ischemic middle cerebral artery stroke, within the first 72 hours of clinical evolution. Thirty-seven EEGs and clinical evaluations were collected: 13 during the first 24 hours after stroke onset, 9 between 24-48 hours and 15 between 48-72 hours. The QEEG studied variables were: the Z values (maximum, minimum and the Z medians from the 5 nearest points to each one) of absolute energies (AE) from the 4 classic frequencies bands. The clinical scale showed a smaller percent of correct prognosis than QEEG variables. CONCLUSIONS: QEEG was demonstrated to be a powerful tool to predict the degree of residual functional disabilities after an acute ischemic stroke and showed a higher prognostic value than CaNS when they are performed within the first 72 hours of brain infarct.

Stroke 2003 Jan;34(1):138-43
**Poststroke depression: an 18-month follow-up.**
Department of Neurology, Helsinki University Central Hospital, Finland (A.B., H.P., M.K.).
Background and Purpose: This prospective study was designed to examine the course, associates, and predictors of depressive symptoms during the first 18 months after stroke.
METHODS: A total of 100 patients were followed up for 18 months after stroke. Depressive symptoms were assessed at 2 weeks and 2, 6, 12, and 18 months after stroke with the **Beck Depression Inventory and the Hamilton Rating Scale for Depression**, and diagnoses were performed using criteria outlined in the **Diagnostic and Statistical Manual of Mental Disorders**, Third Edition-Revised. Stroke severity was assessed with the Scandinavian Stroke Scale and cognitive functions with a comprehensive neuropsychological battery. Patients
participated in a randomized clinical trial of antidepressive medication. RESULTS: In all, 54% of patients felt at least mildly depressive at some time during the follow-up; 46% of those who were depressive during the first 2 months were also depressive at 12 and/or 18 months. Only 12% of patients were depressive for the first time at 12 or 18 months. The male sex was associated with a more negative change in depressive symptoms during the follow-up. Older age was associated with depressive symptoms during the first 2 months, stroke severity from 6 to 12 months, and the male sex at 18 months. Depressive symptoms were unrelated to the lesion location. CONCLUSIONS: Depressive symptoms are frequent and they often have a chronic course. Depression is associated with stroke severity and functional impairment, and with the male sex at 18 months. Attention should be focused on the long-term prognosis of mood disturbances and adaptation.

J Affect Disord 2003 Jan;73(1-2):133-46

Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania.
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BACKGROUND: The boundaries of bipolarity have been expanding over the past decade. Using a well characterized epidemiologic cohort, in this paper our objectives were: (1) to test the diagnostic criteria of DSM-IV hypomania, (2) to develop and validate criteria for the definition of softer expressions of bipolar-II (BP-II) disorder and hypomania, (3) to demonstrate the prevalence, clinical validity and comorbidity of the entire soft bipolar spectrum. METHODS: Data on the continuum from normal to pathological mood and overactivity, collected from a 20-year prospective community cohort study of young adults, were used. Clinical validity was analysed by family history, course and clinical characteristics, including the association with depression and substance abuse. RESULTS: (1) Just as euphoria and irritability, symptoms of overactivity should be included in the stem criterion of hypomania; episode length should probably not be a criterion for defining hypomania as long as three of seven signs and symptoms are present, and a change in functioning should remain obligatory for a rigorous diagnosis. (2) Below that threshold, 'hypomanic symptoms only' associated with major or mild depression are important indicators of bipolarity. (3) A broad definition of bipolar-II disorder gives a cumulative prevalence rate of 10.9%, compared to 11.4% for broadly defined major depression. A special group of minor bipolar disorder (prevalence 9.4%) was identified, of whom 2.0% were cyclothymic; pure hypomania occurred in 3.3%. The total prevalence of the soft bipolar spectrum was 23.7%, comparable to that (24.6%) for the entire depressive spectrum (including dysthymia, minor and recurrent brief depression). LIMITATION: A national cohort with a larger number of subjects is needed to verify the numerical composition of the softest bipolar subgroups proposed herein. CONCLUSION: The diagnostic criteria of hypomania need revision. On the basis of its demonstrated clinical validity, a broader concept of soft bipolarity is proposed, of which nearly 11% constitutes the spectrum of bipolar disorders proper, and another 13% probably represent the softest expression of bipolarity intermediate between bipolar disorder and normality.
A new brain-computer interface design using fuzzy ARTMAP.
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This paper proposes a new brain-computer interface (BCI) design using fuzzy ARTMAP (FA) neural network, as well as an application of the design. The objective of this BCI-FA design is to classify the best three of the five available mental tasks for each subject using power spectral density (PSD) values of electroencephalogram (EEG) signals. These PSD values are extracted using the Wiener-Khinchine and autoregressive methods. Ten experiments employing different triplets of mental tasks are studied for each subject. The findings show that the average BCI-FA outputs for four subjects gave less than 6% of error using the best triplets of mental tasks identified from the classification performances of FA. This implies that the BCI-FA can be successfully used with a tri-state switching device. As an application, a proposed tri-state Morse code scheme could be utilized to translate the outputs of this BCI-FA design into English letters. In this scheme, the three BCI-FA outputs correspond to a dot and a dash, which are the two basic Morse code alphabets and a space to denote the end (or beginning) of a dot or a dash. The construction of English letters using this tri-state Morse code scheme is determined only by the sequence of mental tasks and is independent of the time duration of each mental task. This is especially useful for constructing letters that are represented as multiple dots or dashes. This combination of BCI-FA design and the tri-state Morse code scheme could be developed as a communication system for paralyzed patients.

Impaired Recognition of Social Emotions following Amygdala Damage.
Adolphs R, Baron-Cohen S, Tranel D.
University of Iowa.

Lesion, functional imaging, and single-unit studies in human and nonhuman animals have demonstrated a role for the amygdala in processing stimuli with emotional and social significance. We investigated the recognition of a wide variety of facial expressions, including basic emotions (e.g., happiness, anger) and social emotions (e.g., guilt, admiration, flirtatiousness). Prior findings with a standardized set of stimuli indicated that recognition of social emotions can be signaled by the eye region of the face and is disproportionately impaired in autism (Baron-Cohen, Wheelwright, & Jolliffe, 1997). To test the hypothesis that the recognition of social emotions depends on the amygdala, we administered the same stimuli to 30 subjects with unilateral amygdala damage (16 left, 14 right), 2 with bilateral amygdala damage, 47 brain-damaged controls, and 19 normal controls. Compared with controls, subjects with unilateral or bilateral amygdala damage were impaired when recognizing social emotions; moreover, they were more impaired in recognition of social emotions than in recognition of basic emotions, and, like previously described patients with autism, they were impaired also when asked to recognize social emotions from the eye region of the face alone. The findings suggest that the human amygdala is relatively specialized to process stimuli with complex social
significance. The results also provide further support for the idea that some of the impairments in social cognition seen in patients with autism may result from dysfunction of the amygdala.

Brain Inj 2003 Mar;17(3):189-98
Cognitive and affective sequelae in complicated and uncomplicated mild traumatic brain injury.
Borgaro SR, Prigatano GP, Kwasnica C, Rexer JL.
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This study examined cognitive and affective disturbances in patients with complicated (presence of space occupying lesion) vs uncomplicated (absence of space occupying lesion) mild traumatic brain injury (TBI). It was predicted that the complicated group would perform worse in both domains compared to the uncomplicated group. Participants were 28 patients admitted to an inpatient neurorehabilitation unit with mild TBI and assessed within 40 days of their injury. The complicated group (n = 14) was matched to the uncomplicated group (n = 14) on Glasgow Coma Scale score and compared to 14 normal controls on the BNI Screen for Higher Cerebral Functions (BNIS). The complicated group showed greater cognitive disturbances than the uncomplicated and control groups, while both TBI groups performed worse on affective measures. These findings document the role of affective disturbances in mild TBI. They also highlight the importance of early intervention strategies for improving affective communication in patients with mild TBI.

Journal of Neurology Neurosurgery and Psychiatry 2003;74:326-332
A study of persistent post-concussion symptoms in mild head trauma using positron emission tomography
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Brain Inj 2003 Jan;17(1):73-8
Olfactory function after mild traumatic brain injury.
Department of Neurology, University Hospital Maastricht, Maastricht, The Netherlands.
Objective: The aim of this study was to determine the incidence of olfactory dysfunction after mild traumatic brain injury (MTBI). Damage to the olfactory bulbs or frontal cortex has been reported in MTBI, but olfactory dysfunction after MTBI has not been studied in a prospective way before. Design: Patients with first-time MTBI were included. Patients' olfactory threshold values (Hyposmia Utility Kit by Olfacto-Labs(R)) were measured 2 weeks after the trauma. Associations between olfactory threshold values and individual symptoms and S-100B and NSE concentrations were examined, using multiple linear regression analysis, adjusting for the influence of age. Results: Twenty-two per cent of 111 included patients had hyposmia and 4% had anosmia. Thresholds at 2 weeks showed no significant associations with the presence of symptoms at the ER, nor with early concentrations of S-100B or NSE. Conclusions: Although a high prevalence of olfactory dysfunction was found, no correlation was found between olfactory dysfunction and acute parameters of MTBI.

(Replication of Thatcher’s several previous studies...)

...lowering of the connectivity patterns in the beta1 and beta2 frequencies (phase and coherences) and increases predominantly in the relative power of beta1 (13–32 Hz), which were correlated with the differences in recall. There is a subtle shift to right hemisphere/right temporal functioning and employment of the higher beta1 and beta2 frequencies (phase and coherence) in the response pattern of the MTBI subject. Memory functioning is predominantly positively correlated with connection activity (phase and coherence) and negatively correlated with beta activation at specific locations.

Archives of Clinical Neuropsychology
Volume 18, Issue 4, May 2003, Pages 397-417

Soccer heading frequency predicts neuropsychological deficits*
Adrienne D. Witol and Frank M. Webbe,
This study investigated the presence of neuropsychological deficits associated with hitting the ball with one's head (heading) during soccer play. A neuro-cognitive test battery was administered to 60 male soccer players, high school, amateur and professional level, and 12 nonplaying control participants. The effects of currently reported heading behavior as well as that of estimated lifetime heading experience on neuropsychological test performance were examined. Players with the highest lifetime estimates of heading had poorer scores on scales measuring attention, concentration, cognitive flexibility and general intellectual functioning. Players' current level of heading was less predictive of neuro-cognitive level. Comparison of individual scores to age-appropriate norms revealed higher probabilities of clinical levels of impairment in players who reported greater lifetime frequencies of heading. Because of the worldwide popularity of the game, continued research is needed to assess the interaction between heading and soccer experience in the development of neuropsychological deficits associated with soccer play.
Electrophysiology of the frontal lobe.
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The electrophysiology of the frontal lobe appears to be unimpressive when the view is limited to the routine EEG recording of a healthy waking adult. There is usually low voltage fast activity, which becomes more pronounced when recorded with depth leads. Three special EEG patterns of marginal to slightly abnormal character are discussed: a) rhythmical midfrontal 6-7/sec activity of juveniles, b) rhythmical midfrontal sharp 4-6/sec activity of infancy and early childhood with arousal from sleep, and c) frontal intermittent rhythmical delta activity (FIRDA) in waking adults with frontopolar maximum, possibly related to thought processes under abnormal conditions. With extension of the frequency range, ultraslow (DC-like) as well as fast beta (gamma, 40-80/sec) and ultrafast activity (80-1000/sec) are found particularly over the frontal lobes. Ultraslow baseline shifts are arousal-related and mixed with overlying ultrafast waves. Attention control and the "working memory" involve chiefly the dorsolateral prefrontal cortex, investigated with P300 responses and likely to show ultrafast spectra. Perception-related 40-80/sec gamma activity has been thought to be associated with the entrance into consciousness. Initiation and design of motor activity spreads from prefrontal to the frontomotor cortex, associated with powerful event-related potentials: contingent negative variation (CNV) and "Bereitschafts potential" ("readiness potential," RP). Neuroscientific research of the highest frontal lobe functions has become a very active domain of neuroimaging. With the use of the extended frequency range, EEG and also evoked potential studies could add further information with acquisition in real time. Ultrafast frequency ranges presented in computerized frequency analysis and mapping might show impressive correlates of highest frontal lobe functions.

Are there sub-types of attentional deficits in patients with persisting post-concussive symptoms? A cluster analytical study.
Chan RC, Hoosain R, Lee TM, Fan YW, Fong D.
Department of Psychiatry, the University of Hong Kong, Hong Kong, PR China.
Aim: The present study aimed to examine attentional deficits in patients with persisting post-concussive symptoms using a multi-componential framework of attention. Design: A cross-sectional investigation using standardized tests and questionnaires of attention including 92 patients. Method: Participants were administered comprehensive measures of attention assessing sustained attention (Sustained Attention Response to Task, Backward Digit Span), selective attention (Stroop Word-Colour Test, Colour Trails Test), divided attention (Paced Auditory
Serial Addition Test, Symbol Digit Modalities Test), and attentional control (Tower of Hanoi, Six Elements Test). Ecological tests of attention were used to validate the cluster solution. Main outcome: Three clusters of patients with different combinations of attentional deficits were identified. They were 'mild sustained attentional deficits', 'selective and divided attentional deficits', and 'general attentional deficit'. A MANOVA indicated that these three clusters were statistically and clinically different from one another in terms of different attentional components proposed. Conclusion: This study provides preliminary evidence suggesting that sub-types of attentional impairments exit in patients with post-concussive symptoms.
Congenital and acquired brain injury. 4. New frontiers: neuroimaging, neuroprotective agents, cognitive-enhancing agents, new technology, and complementary medicine.

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This self-directed learning module explores the clinical application of new and evolving research frontiers in the field of neuroimaging, neuroprotective agents, and cognition-enhancing medications as applied to patients with brain injury. The current and potential clinical applications of robotic technology, virtual reality, and telemedicine in the field of physical medicine and rehabilitation is explored. The evidence to support a growing interest in and application of complementary medicine techniques in brain injury and other disorders is reviewed.

OVERALL ARTICLE OBJECTIVES: (a) To explore the current research and potential clinical applications of medical and technologic advances in neuroprotective agents, cognition-enhancing agents, neuroimaging, virtual reality, robotics, and telemedicine as applicable to brain injury and (b) to identify the evidence to support an expanding use of complementary medicine in brain injury.

Correlation between electroencephalography and heart rate variability during sleep.

Biofunctional Informatics, Graduate School of Allied Health Sciences, Tokyo Medical and Dental University, Department of Sleep Disorders Research, Tokyo Institute of Psychiatry, Department of Cardiovascular Medicine, Tokyo Medical and Dental University, Tokyo, Japan and Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, USA.

It is known that autonomic nervous activities change in correspondence with sleep stages. However, the characteristics of continuous fluctuations in nocturnal autonomic nerve tone have not been clarified in detail. The study aimed to determine the possible correlation between the electroencephalogram (EEG) and autonomic nervous activities, and to clarify in detail the nocturnal fluctuations in autonomic nerve activities. Overnight EEGs and electrocardiograms of seven healthy males were obtained. These EEGs were analyzed by fast Fourier transformation algorithm to extract delta, sigma and beta power. Heart rate and heart rate variability (HRV) were calculated in consecutive 5-min epochs. The HRV indices of low frequency (LF), high frequency (HF) and LF/HF ratio were calculated from the spectral analysis of R-R intervals. The sleep stages were manually scored according to Rechtschaffen and Kales' criteria. Low frequency and LF/HF were significantly lower during non-rapid eye movement (NREM) than REM, and were lower in stages 3 and 4 than in stages 1 and 2. Furthermore, delta EEG showed inverse correlations with LF (r = - 0.44, P < 0.001) and LF/HF (r = - 0.41, P < 0.001). In
contrast, HF differed neither between REM and NREM nor among NREM sleep stages. Detailed analysis revealed that correlation was evident from the first to third NREM, but not in the fourth and fifth NREM. Delta EEG power showed negative correlations with LF and LF/HF, suggesting that sympathetic nervous activities continuously fluctuate in accordance with sleep deepening and lightening.

Recent developments in the psychobiology and pharmacotherapy of depression: optimising existing treatments and novel approaches for the future.
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Effective antidepressants include monoamine oxidase inhibitors and tricyclic antidepressants, selective serotonin re-uptake inhibitors and novel agents, including serotonin and noradrenaline re-uptake inhibitors. Although effective, current treatments most often produce partial symptomatic improvement (response) rather than symptom resolution and optimal functioning (remission). While current pharmacotherapies target monoaminergic systems, different symptoms of major depressive disorder (MDD) may have distinct neurobiological underpinnings and other neurobiological systems are likely involved in the pathogenesis of MDD. In this article a review of current pharmacotherapeutic options for MDD, current understanding of the neurobiology and pathogenesis of MDD and a review of new and promising directions in pharmacological research will be provided. It is generally accepted that no single neurotransmitter or system is responsible for the dysregulation found in MDD. While agents that affect monoaminergic systems will likely continue to be first-line treatments for MDD for the foreseeable future, a number of new and novel agents, including corticotropin-releasing factor antagonists, substance P antagonists and antiglucocorticoids show considerable promise for refining treatment options. In order to better understand the neurobiology and treatment response of MDD, it is probable that more sophisticated theory-driven typologies of MDD will have to be developed.

ADHD and conduct disorder: an MRI study in a community sample.

Compliance with stimulants for ADHD

Childhood Autism Rating Scale - screening pervasive developmental disorders.
Reported problems following traumatic brain injury amongst children in UK.

Measurement of impaired self-awareness after traumatic brain injury

Brain injury and violent crime.

Outcome of prolonged coma following severe TBI.
BioMed Central - The Open Access Publisher Newsletter - Update
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PSYCHOTHERAPY

"In an award winning paper, research L. Bickman (1999) identified several popular beliefs held by practicing psychotherapists and the field in general regarding the effectiveness of treatment. Briefly, he found no empirical support for the ideas that effectiveness was assured by (1) experienced clinicians; (2) continuing education; (3) professional degree; (4) licensing; (5) accreditation; or (6) clinical supervision. Importantly, this does not mean that psychotherapy as practiced is ineffective. Rather, it underscores the idea that effective care has little to do with the stuff that continues to dominate professional discourse, training, and practice; that is treatment models and methods."


From
www.talkingcure.com

FORWARD:

I posted a link to www.talkingcure.com several days ago for a number of reasons.

So much of the recent discussion on this list has hinged around the contention that 1) my protocol is better than yours in that people get better more quickly and are happier with the outcome (based as many have noted on virtually no data) and 2) George's repetetive rants on professional certification etc. citing Garb and Dawes.

Dr. Miller's site has something to offer on both of these topic areas and raises important questions as to what is going on in any therapeutic interaction, including eeg bf. When one admits to significant behavioral/emotional/cognitive changes after treatment, but cannot point to any reliable consistent physical marker corresponding to this change, it becomes even more important to look at 40 years of psychotherapy outcome research. Citations for the material below can be found at the site.

A few relevant findings mentioned by Dr.Miller include:

"Since the mid-1960's, the number of therapy models has grown from 60 to more than 250. At the same time, virtually all of the research data finds that the various treatment approaches achieve roughly equivalent results. This is true of both the biological and well as the much bally-hoed cognitive and cognitive behavioral revolutions. When all is said and done, virtually all of the data find that the various approaches work about equally well."

"Research points to the existence of four factors common to all forms of therapy despite theoretical orientation (dynamic, cognitive, etc.), mode (individual, group, couples, family, etc.),
Might a huge amount of practitioner success be attributable to extratherapeutic factors, including those specific to the practitioner? Dr. Von's encouraging pats and grandfatherly demeanor...the expectation of someone coming to Val Brown, that this is a no-nonsense serious guy who will get the job done...etc etc.

Might the best practitioners be those who are best at picking their clients -- or practitioners who have such a well-established theory of change that clients having the same theory pick the practitioner most aligned with their beliefs.

Given much outcome research suggesting that therapeutic structure/model/technique accounts for only about 15% of observed change, is it fruitful to stay so obsessively focused on the hardware/software and unsupported claims of greater efficacy? I would welcome more discussion about what gets patients into EEG b/ training, what keeps them there and what sort of interactions take place between practitioner and client.

From: Dave Giffen
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REHABILITATION

TORONTO STAR
www.thestar.com
Jan. 2, 2003. 05:01 PM

Sex function in brain could aid stroke victims
HELEN BRANSWELL
CANADIAN PRESS
Mating triggers the development of new neurons in the smell centre of the brain, a finding researchers hope will provide clues on how to trick other parts of the vital organ to repair themselves after injuries caused by strokes or head traumas. The possibility hinges on the discovery that a naturally occurring hormone called prolactin -- production of which surges after sex and during pregnancy -- prompts stem cells in the brain to produce new neurons in the brain's...
olfactory bulb. "The importance of it, beyond the basic biology of stem cells, is the fact that prolactin may be an important neurogenic molecule that may have significant potential for generating new brain cells," said Samuel Weiss, an expert in neurological stem cell biology in the University of Calgary's faculty of medicine. Weiss is the senior author of the study, published Friday in the journal Science. The work was a collaboration between his laboratory and that of James Cross, also part of the genes and development research group at the University of Calgary. The researchers were building on a discovery Weiss reported about a decade ago, that the brains of adult mice contain stem cells that are the body's building blocks. Stem cells have the capacity to turn into any type of cell. Later it was shown that the adult human brain contains stems cells as well. Those findings were considered monumental, because it had long been believed that the brain cannot generate new cells to replace or repair those lost to injury. Over time, Weiss and his colleagues determined that the major role of these stem cells was to produce new neurons for the brain cells that communicate with one another for the olfactory bulb. The stem cells are located in another part of the brain and the neurons they produce have to migrate to the olfactory bulb. Once there they "differentiate," meaning they mature into a specific type of cell in this case olfactory bulb neurons. Further work showed that female mice which were genetically engineered to contain fewer stem cells and therefore fewer new neurons in the olfactory bulb were less attentive mothers to their offspring. It is well established that the sense of smell is crucial to mating and to rearing offspring, allowing both animals and insects to recognize their mates and progeny. Working with mice, the Calgary researchers determined that there was a spike in olfactory bulb neuron production during the early stages of pregnancy and shortly after birth. The hormone which appears to trigger the production is prolactin, which fuels several key physiological changes in females during pregnancy and after birth. The hormone is also present in males, where it obviously serves a different function. Weiss and his colleagues discovered that prolactin levels and consequently new neuron production surge after mating as well. And they found that if prolactin was introduced to the blood system by injection, it also stimulated production of new neurons for the olfactory bulb. While they aren't certain the same process occurs in human, they do know that sex triggers a surge of prolactin in humans. Weiss acknowledged that some researchers will be interested in their findings because of what they say about mating and the sense of smell. But he and his colleagues want to see whether the process they've found can be altered to send new neurons to other parts of the brain. Another study, published last year in the journal Nature, suggests it may be possible. Researchers working with rats reported that in the case of brain damage some of the stem cells spontaneously redirected new neurons towards the injury, but in numbers too small to repair the damage. If the stem cells could be tricked into directing sufficient numbers of new neurons, "it provides potentially a way to boost the brain's self-repair process and allow for enhanced functional recovery after the stroke," Weiss said, who has been collaborating with Bryan Kolb at the University of Lethbridge to test the theory. "We have exciting preliminary data suggesting that the new stem cell-generated brain cells can be redirected to parts of the rodent brain that are damaged after a stroke and this results in partial improvement of the animal's ability to move its limbs," he said. If the theory is proven, it might also provide clues on how to mitigate the damage done by neurodegenerative diseases such as Parkinson's or Alzheimers. Funding for the work was provided by the Canadian Institutes of Health Research, the Canadian Stroke Network, the Alberta Heritage Foundation for Medical Research, the Multiple Sclerosis Society of Canada and the Stem Cell Network of the Network of Centres of Excellence.
Researchers in Germany have demonstrated that there is a physiological component to a learned behavior that psychologists have recognized for years: People with chronic back pain whose spouses cater to their needs had more brain activity in response to pain stimulation than those whose spouses try to distract them from the pain.

Herta Flor's team measured brain activity with an array of electroencephalogram (EEG) electrodes placed on the patients' heads. They found that when they gave the patients a small painful stimulus in their backs, all ten of the patients who have solicitous spouses had significantly more activity in the anterior cingulate region of their brains than did the ten patients whose spouses were not so attentive. The brain activity difference between the two groups was about threefold.

Interestingly Flor, a neuropsychologist at the University of Heidelberg, and colleagues detected these large brain wave responses only when the patient's spouse was in the same room and when the pain stimulation was directed to the back. The exaggerated response did not occur either when the spouse was in another room, nor when the stimulation was a painful prick to the finger.

Flor said these data fit right in with a long history of research on learned behavior: "Any kind of behavior that is followed by a positive response is going to be strengthened over time. " If every time a patient complains about back pain, the spouse responds with extra attention, by bringing dinner or giving a massage, the patient's brain learns to respond to the pain. But if the spouse offers a distraction such as suggesting a walk, or even if the spouse leaves the room or just doesn't pay attention, the brain has no positive feedback to train a response to the pain or the mere discussion of pain.

This is not a voluntary response, stressed Flor. The excess brain activity occurs on its own and is not under the patient's control - although the researchers are exploring whether they can use biofeedback training to mitigate the brain's response.

Allan Basbaum, a neurophysiologist at the University of California, San Francisco, told BioMedNet News: "I am not at all surprised by the results." He finds it noteworthy that the patients only had this exaggerated response to back pain and not to a pricked finger, indicating that this really is part of the chronic pain pathway and response - not a response involving the acute pain system.
He also said that he thought the location of the brain response was intriguing. The anterior cingulate is known to be involved in processing emotional responses to pain.

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**Novel modulation of NMDA receptor function**
13 January 2003
by Anthony Dickenson anthony.dickenson@ucl.ac.uk

Glutamate is the major excitatory transmitter in the CNS, and there has been considerable interest in the potential therapeutic effects of blocking the complex N-methyl-D-aspartate (NMDA) receptor. There is considerable evidence that the receptor plays a key role in excitotoxicity, epilepsy and persistent pain states; however, agents that block the receptor, channel or modulatory sites have low therapeutic indices that preclude their clinical utility. An alternative approach is to modulate protein–protein interactions so that the coupling of the surface receptor to intracellular proteins and enzymes is disrupted. PSD-95 is a protein that binds the NR2 subunit of the receptor and also neuronal nitric oxide synthase, which mediates several of the functional effects of NMDA receptor activation. This paper reports that a 20 amino acid peptide construct (Tat NR2B9c), rendered cell permeant, can functionally alter NMDA receptor activation by disrupting the PSD-95–receptor interaction. Tat NR2B9c was shown to enter cells and reduce coimmunoprecipitation of the NR2B receptor with PSD-95. This had no effect on either NMDA-evoked currents in neurones or on AMPA receptors, or the calcium flux through the NMDA receptor — these do not rely on PSD-95 interactions. However, downstream events were effected, in that cGMP production was suppressed by the peptide, indicating altered nitric oxide signaling. Tat NR2B9c was then proven to enter the brain after systemic administration. When tested against ischemic brain damage induced by middle cerebral artery occlusion, Tat NR2B9c reduced the volume of tissue in the infarct, which was 70% less in the cortex. Tat NR2B9c was further shown in vitro to be effective when given after NMDA challenge to neurones in culture, and this translated into in vivo activity. Thus, when given 1 h after the onset of experimental stroke, the peptide had better neurological scores than those from control animals, and again reduced infarction volume.

This paper emphasizes the importance of protein–protein interactions and, somewhat surprisingly, reports that a peripherally administered peptide can attenuate, to a major extent, some of the functional aspects of NMDA receptor activation. This approach has implications for other receptors and diseases.

SFN 2002 - Day 1 - Sunday 3 November 2002
Report:
**Nose news for new nerves**
Investigator: Hans Keirstead
3 November 2002
by Apoorva Mandavilli
A unique group of human cells, isolated from the nasal epithelium, can help rats with injured spinal cords recover their ability to walk, US researchers reported today. The approach is one of several in the revitalized field of nerve regeneration.

The prevailing dogma in regeneration holds that "axons grow where the [growth promoting] cells go," said Hans Keirstead, assistant professor of anatomy and neurobiology at the University of California in Irvine. But researchers have not been able to take advantage of that concept because growth-promoting cells generally do not migrate, Keirstead explained.

Embryonic stem cells are one exception to that rule; so are olfactory ensheathing cells (OECs), which enable the sense of smell. OECs grow rapidly, are non-tumorigenic, and unlike most cells of the central nervous system, can replace themselves when injured. When they are transplanted, the cells can also migrate. "That's a rare, rare trait," Keirstead said.

In the past few years, several teams have investigated the ability of OECs to promote axon regeneration and generate new myelin sheaths, primarily with cells derived from canine and rodent olfactory bulbs. The researchers have met with mixed results, ranging from excellent recovery to none at all.

When Keirstead purified OECs from human nasal mucosa and transplanted them into a rat model of severe spinal injury, there was some regrowth of neurons in the injured spinal cords, even in areas with scarring, Keirstead reported. The rats also quickly regained bladder function and regained some of their ability to walk.

"This is the first time human OECs prepared in this high-purity manner have been used to investigate their ability to treat the injured spinal cord," says Keirstead. "Because our study used human cells, it has direct significance for clinical use."

Using human OECs has many advantages. Extraction of the cells is an easy five-minute procedure, and subjects experience no side-effects, apart from temporary hallucinations of smell, Keirstead said. They can also be used in autologous transplants, minimizing most of the complications associated with transplantation.

OECs are only one of several new promising techniques in regeneration. At the University of Utah, researcher Ray Lund and his colleagues have transplanted a human pigment epithelial cell line and improved vision in a rat model of retinal degeneration.

Yale University researchers, led by neurobiologist Stephen Strittmatter, have developed a synthetic peptide that blocks the Nogo gene, which inhibits regeneration. The peptide promotes new nerve fiber growth in the damaged spinal cords of laboratory rats, allowing them to walk better, Strittmatter said.

Before any of these therapies can be moved to human trials, however, they must first undergo extensive testing for safety and efficacy in human disease.
If scientists can take cues from brain development to devise the right combination of growth promoting cells and neurotrophic factors, they may be able to promote neuronal regeneration, said Keirstead. But, he said, "there's still a lot going on in brain development that we don't understand."

This morning's Washington Post carries an article, "FDA Approves Prozac for Kids."

Here are a few excerpts, which notes research findings that "children and teenagers taking Prozac grew a little more slowly -- a half inch less in height and two pounds less in weight over a period of 19 weeks -- than similarly aged children taking a dummy pill."

[begin excerpts]

[Prozac] is the first drug among the newer antidepressants, which boost the mood regulator serotonin, to win [FDA] approval [for children 8 years old and older].

But children have a unique side effect: In one study, children and teenagers taking Prozac grew a little more slowly -- a half inch less in height and two pounds less in weight over a period of 19 weeks -- than similarly aged children taking a dummy pill.

As much as 25 percent of U.S. children and 8 percent of teenagers have depression, the FDA said. Additionally, about 2 percent of the population has obsessive-compulsive disorder, and at least a third of those cases began in childhood.

[end excerpts]


If that address is too long for your browser or doesn't work, try going to the Post's home page at [http://www.washingtonpost.com](http://www.washingtonpost.com) and finding it from
Anne Lamott, quoting a friend's 5 Rules For Living:

1. Be born perfect, without imperfection or any significant differences from the majority that might make others uncomfortable.

2. If you have imperfections or are different in any way, get it fixed immediately.

3. If you can't get it fixed, at least act as if it has been fixed.

4. If you can't act as if it has been fixed, then don't show up.

5. If you must show up, at least have the decency to be ashamed.

Some of these might be the nootropics of the future. Idebenone is mentioned. A complete explanation of the mechanisms of action of drugs that regenerate nervous tissue...

Http://www.bentham.org/cdtnsnd1-1/pollack/pollack-ms.htm


Object-based representations facilitate memory for inhibitory processes
Matthew A. Paul and Steven P. Tipper,
School of Psychology, Centre for Cognitive Neuroscience, University of Wales, Bangor, Gwynedd LL57 2AS, UK

Previous work has shown that in a sequential cueing task, inhibition of the return of attention (IOR) can be observed for up to four or five loci. We have argued that the inhibition processes mediating IOR are associated with object-based representations, and it is object-based representations that are maintained in memory. Experiments presented here show that, compared with standard conditions in which a number of identical grey squares are cued, cueing empty locations tends to reduce the memory for prior inhibitory processes; while cueing objects which are distinctive in colour and shape tends to increase memory for inhibition. Converging with
other recent findings, we conclude that memory for the inhibitory processes of attention facilitates visual search and that this memory is dependent on object-based representations.


Proprioceptive sensory function in Parkinson's disease and Huntington's disease: evidence from proprioception-related EEG potentials
E. Seiss, P. Praamstra1, C. W. Hesse and H. Rickards3
Behavioural Brain Sciences Centre, University of Birmingham, Birmingham B15 2TT, UK
Department of Clinical Neurosciences, Queen Elizabeth Hospital, University of Birmingham, Birmingham, UK
Department of Psychiatry, Queen Elizabeth Hospital, University of Birmingham, Birmingham, UK

Abstract. In both Parkinson's disease and Huntington's disease, proprioceptive sensory deficits have been suggested to contribute to the motor manifestations of the disease. Here, proprioceptive sensory function was investigated in Parkinson's disease patients, Huntington's disease patients, and healthy control subjects (each group n=8), using proprioception-related evoked potentials. Proprioception-related potentials were elicited by passive index finger movements and measured with high-density EEG. Conventional median nerve somatosensory evoked potentials (mnSEPs) were recorded in the same session. Analysis included amplitude and latency measures from selected scalp electrodes and dipole source reconstruction. We found a proprioception-related N90 component of normal latency in both Parkinson's disease and Huntington's disease. The source strength of the underlying cortical generator was normal in Parkinson's disease, but marginally reduced in Huntington's disease. Using the source location of the N20- P20 component of the mnSEP as a landmark for postcentral area 3b, the N90 was localized to the precentral motor cortex. At a latency around 170-180 ms proprioception-related potentials were explained by bilateral sensory cortex activation with an altered distribution in Parkinson's disease and a reduction of ipsilateral activation in Huntington's disease. Together, the results show largely normal early proprioception-related potentials, but changes in the cortical processing of kinaesthetic signals at longer latencies in both diseases.

Archives of Clinical Neuropsychology
Volume 18, Issue 1, January 2003, Pages 1-9

Detecting malingering on the WAIS-III
Unusual Digit Span performance patterns in the normal population and in clinical groups
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b Neuropsychiatry Units at Riverview Hospital, Port Coquitlam, BC, Canada
c Spinal Cord Injury Research Laboratory at Kessler Medical Rehabilitation Research and Education Corporation, West Orange, NJ, USA

Abstract
In several studies, suppressed Digit Span performance has been proposed as a potential marker for deliberately poor performance in a neuropsychological evaluation. The purpose of this study was to document Digit Span performance patterns in the Wechsler Adult Intelligence Scale—
Third Edition (WAIS-III; Wechsler, 1997) standardization sample and selected clinical groups. Base rate tables were generated for the Digit Span scaled score, longest span forward, longest span backward, and the Vocabulary–Digit Span difference score. Cut-off scores for suspecting negative response bias were proposed, and clinical case examples were used to illustrate these scores.

**Use of the CBDI to detect malingering when malingers do their "homework"
**
Archives of Clinical Neuropsychology Volume 18, Issue 1 January 2003 Pages 57-69
Jeffrey J. Borckardt, , a, Eric S. Engum, E. Warren Lambert, Michael Nasha, Odie L. Braeyd and Edward C. Raya

Previous research has demonstrated the ability of the Cognitive Behavioral Driver's Inventory (CBDI) to detect neuropsychological malingering [Arch. Clin. Neuropsychol. 12 (5) (1997) 491.], however, the present study tests if the CBDI can discern malingers when they are "coached" on how brain-damaged patients actually perform on neuropsychological tests. Ninety-eight college student participants were given financial incentive to fake brain damage on the CBDI. Fifty-three of these subjects were "coached" and 45 were not. The coached and uncoached subjects performed indistinguishably on the CBDI. Both types of malingers were discernable from real brain-damaged patients (99.2% accuracy area under the sensitivity–specificity curve). Further, CBDI profiles of five actual plaintiffs judged to be malingering were compared to CBDI profiles of experimental subjects. In each case, the malingering plaintiff's CBDI profile was indistinguishable from that of malingering experimental subjects and was clearly discernable from that of actual brain-damaged patients.

**Partial cross-validation of the Wechsler Memory Scale—Revised (WMS-R) General Memory—Attention/Concentration Malingering Index in a nonlitigating sample
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Archives of Clinical Neuropsychology Volume 18, Issue 1 January 2003 Pages 71-79
Robin C. Hilsabeck, , a, b, Matthew D. Thompson, c, James W. Irby, d, Russell L. Adams, James G. Scotta and Wm. Drew Gouvier

The Wechsler Memory Scale—Revised (WMS-R) malingering indices proposed by Mittenberg, Azrin, Millsaps, and Heilbronner [Psychol Assess 5 (1993) 34.] were partially cross-validated in a sample of 200 nonlitigants. Nine diagnostic categories were examined, including participants with traumatic brain injury (TBI), brain tumor, stroke/vascular, senile dementia of the Alzheimer's type (SDAT), epilepsy, depression/anxiety, medical problems, and no diagnosis. Results showed that the discriminant function using WMS-R subtests misclassified only 6.5% of the sample as malingering, with significantly higher misclassification rates of SDAT and stroke/vascular groups. The General Memory Index—Attention/Concentration Index (GMI-ACI) difference score misclassified only 8.5% of the sample as malingering when a difference score of greater than 25 points was used as the cutoff criterion. No diagnostic group was significantly more likely to be misclassified. Results support the utility of the GMI-ACI difference score, as well as the WMS-R subtest discriminant function score, in detecting malingering.
Does active leisure protect cognition? Evidence from a national birth cohort
Marcus Richards, Rebecca Hardy and Michael E. J. Wadsworth
Social Science & Medicine Volume 56, Issue 4 February 2003 Pages 785-792

Social, physical and intellectual activities are thought to facilitate cognitive performance and slow the rate of age associated cognitive decline, but little is known about this association in younger adulthood. We used multiple regression to test the association between two kinds of activity at 36 years—physical exercise and spare-time activity—and verbal memory at 43 and 53 years in 1919 males and females enrolled in the MRC National Survey of Health and Development (the British 1946 birth cohort). Both kinds of activities were significantly and positively associated with memory performance at 43 years, after controlling for sex, education, occupational social class, IQ at 15 years, and recurrent ill health and significant mental distress. Furthermore, physical exercise at 36 years (but not spare-time activity) was associated with a significantly slower rate of decline in memory from 43 to 53 years, after controlling for the same factors, with evidence that continuing physical exercise after 36 years was important for protection. We conclude that physical exercise and spare-time activity are significantly associated with benefit to memory in midlife, although these two kinds of voluntary activity may exert their effects on cognition via different paths.

Inappropriate association of semantics and context to novel stimuli can give rise to the false recognition of unfamiliar people
Jamie Ward, a and Luke Jonesb
Neuropsychologia Volume 41, Issue 5 2003 Pages 538-549

This paper reports further experiments with a patient (MR) who has a tendency to claim that unfamous people are familiar together with good ability at identifying truly famous people. The first experiment examines the role that the typicality of stimuli plays in his false recognition. Although, typicality may have some influence over false recognition (as it does for normal controls) there is little evidence to suggest that MR is over-reliant on such information. It is unlikely that perceptual fluency can entirely explain his deficit. This is bolstered by a further study using morphed images of famous and unfamous faces, suggesting that false recognition is associated with inappropriate retrieval of semantic-biographical information. It is argued that MR's judgement of `fame' is subjectively appropriate, given the information that he retrieves. This information is thought to derive from currently activated, or recently activated, contextual information which becomes inappropriately bound to the novel stimulus, giving rise to a false sense of familiarity. These findings underscore the importance of viewing memory as an attributional process, whereby current mental constructions/processes are attributed to some event(s) in the past.

Theory of mind and psychopathy: can psychopathic individuals read the `language of the eyes'?
R. A. Richellb, D. G. V. Mitchella, b, C. Newmanb, A. Leonarde, S. Baron-Cohend and R. J. R. Blair
here have been suggestions that Theory of Mind (ToM) impairment might lead to aggressive behaviour and psychopathy. Psychopathic and matched non-psychopathic individuals, as defined by the Hare Psychopathy Checklist [The Hare Psychopath Checklist-Revised, 1991] completed the 'Reading the Mind in the Eyes' ToM Test [Journal of Child Psychology and Psychiatry, 1997;38:813]. This test requires the self-paced identification of mental states from photographs of the eye region alone. Results indicated that the psychopathic individuals did not present with any generalised impairment in ToM. The data are discussed with reference to the putative neural system mediating performance on this task and models of psychopathy.

Impairment of recognition of disgust in Chinese with Huntington's or Wilson's disease

Kai Wang, a, Rumjahn Hoosainb, Ren-Min Yangc, Yu Menga and Chang-Qing Wanga

The selective involvement of the basal ganglia in recognition of the facial expression of disgust was investigated by examining a group of six symptomatic Huntington's disease patients and 32 Wilson's disease patients in China. Morphed photographs of facial expressions covering happiness–surprise–fear–sadness–disgust–anger were used and the patients were asked to label each photo. Other measures assessed basic cognitive functions and perception of non-emotion facial information, such as perception of gender, age, gaze direction, and recognition of unfamiliar as well as famous people. There was dissociation between the perception of emotions and other facial information, and between impairment of recognition of disgust and other emotions. The basal ganglia are the overlapping substrate involved in both Huntington's and Wilson's disease, although each has its own other lesions. The differentially severe impairment of recognition of disgust in the Chinese Huntington's disease and Wilson's disease patients strengthens the view that basal ganglia are selectively involved in processing the emotion of disgust.

The anatomy and time course of semantic priming investigated by fMRI and ERPs

Susan L. Rossell, a, Cathy J. Priceb and A. Christina Nobreb

We combined complementary non-invasive brain imaging techniques with behavioural measures to investigate the anatomy and time course of brain activity associated with semantic priming in a lexical-decision task. Participants viewed pairs of stimuli, and decided whether the second item was a real word or not. There were two variables, the semantic relationship between the prime and the target (related or unrelated) and the interval between the onset of prime and target (200 or 1000 ms), to vary the degree of semantic expectancy that was possible during task performance. Behavioural results replicated the well-established finding that identification of the target is facilitated by a preceding semantically related prime. Event-related functional magnetic resonance imaging (efMRI) identified two brain areas involved in the semantic-priming effect. Activity in the anterior medial temporal cortex was diminished when target words were primed by semantically related words, suggesting involvement of this brain region during active semantic association or integration. In contrast, activity in the left supramarginal gyrus in the temporal-parietal junction was enhanced for target words primed by semantically related words.
Brain areas influenced by the interval between prime and target words, and by the interaction between word interval and semantic priming were also identified. A parallel experiment using event-related potentials (ERPs) unveiled a striking difference in the time course of semantic priming as a function of expectancy. In line with previous reports, the primary effect of semantic priming on ERPs was the attenuation of the N400 component, in both short- and long-interval conditions. However, the priming effect started significantly earlier in the long-interval condition. Activity in the anterior medial temporal cortex has previously been shown to contribute to the N400 component, a finding that links the priming results obtained with efMRI and ERP methods.

**Temporary and permanent signs of interhemispheric disconnection after traumatic brain injury**

Neuropsychologia Volume 41, Issue 5 2003 Pages 634-643
Andrea Perua, Alberto Beltramello, Valentina Moroc, Lorenzo Sattibaldic and Giovanni Berlucchi, a

The corpus callosum is frequently damaged by closed head traumas, and the resulting deficits of interhemispheric communication may vary according to the specific position of the lesion within the corpus callosum. This paper describes a single case who suffered a severe traumatic brain injury resulting in a lesion of the posterior body of the corpus callosum. Among the classical symptoms of interhemispheric disconnection, left hand anomia, left upper limb ideomotor dyspraxia, left visual field dyslexia and dysnomia, and left ear suppression in a dichotic listening task were observed shortly after the injury but recovered completely or almost completely with the passage of time. The only symptom of interhemispheric disconnection which was found to persist more than 4 years after the injury was an abnormal prolongation of the crossed-uncrossed difference in a simple visuomotor reaction time task. This prolongation was comparable with that observed in subjects with complete callosal lesions or agenesis. The results suggest that the posterior body of the corpus callosum may be an obligatory interhemispheric communication channel for mediating fast visuo-motor responses. The transient nature of other symptoms of interhemispheric disconnection suggests a relatively wide dispersion of fibers with different functions through the callosal body, such that parts of them can survive a restricted lesion and allow functional recovery of hemispheric interactions. An assessment of the evolution in time of symptoms of interhemispheric disconnection following restricted callosal lesions may reveal fine and coarse features of the anatomo-functional topography of the corpus callosum.

Reality monitoring and visual hallucinations in Parkinson's disease
J. Barnes, L. Boubert, J. Harris, A. Lee, A.S. David
pp 565-574
http://www.sciencedirect.com/science?ob=GatewayURL&origin=CONTENTS&method=citationSearch&_piikey=S0028393202001823&_version=1&md5=58861813bdd2d412064ae556fe5b6c38

Cognitive estimation in patients with probable Alzheimer's disease and alcoholic Korsakoff patients
An fMRI study investigating cognitive modulation of brain regions associated with emotional processing of visual stimuli
M.L. Keightley, G. Winocur, S.J. Graham, H.S. Mayberg, S.J. Hevenor, C.L. Grady
pp 585-596
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202001999&_version=1&md5=ba9c61b25a9a1aabdf72d7228df0d4f7

Interhemispheric visual interaction in a patient with posterior callosectomy
S.R. Afraz, L. Montaser-Kouhsari, M. Vaziri-Pashkam, F. Moradi
pp 597-604
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002014&_version=1&md5=3331d0f96fca51c889bb757f97f17e1f

Perception and production of facial and prosodic emotions by chronic CVA patients
S. Charbonneau, B.P. Scherzer, D. Aspirot, H. Cohen
pp 605-613
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002026&_version=1&md5=d42b747800163d9f3b44b6c786efdf6a7

Ideomotor limb apraxia in Huntington's disease: implications for corticostriate involvement
J.M. Hamilton, K.Y. Haaland, J.C. Adair, J. Brandt
pp 614-621
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S002839320200218X&_version=1&md5=f6602a4aa02e2ec79d875c7d1ebcbdc6

Vision for spatial perception and vision for action: a dissociation between the left-right and near-far dimensions
Y. Coello, S. Richaud, P. Magne, Y. Rossetti
pp 622-633
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002002&_version=1&md5=c1e02bac9df829967d8f9255242208c5
**Feigning /= Malingering.**  
Researchers and scholars assert that feigning should not be equated with malingering. Some practicing clinicians doing the everyday work of forensic assessment may view this as merely an academic distinction. This case study illustrates that a high level of certainty about feigning must not be considered indicative of malingering. The case also contrasts two models for assessing malingering and highlights the need for forensic examiners to present assessment-of-malingering data clearly and cautiously.

**On the pathophysiology of migraine--links for "empirically based treatment" with neurofeedback.**  
Kropp P, Siniatchkin M, Gerber WD.  
Institute of Medical Psychology, University of Kiel, Niemannsweg 147, D-24105 Kiel, Germany. kropp@med-psych.uni-kiel.de  
Psychophysiological data support the concept that migraine is the result of cortical hypersensitivity, hyperactivity, and a lack of habituation. There is evidence that this is a brain-stem related information processing dysfunction. This cortical activity reflects a periodicity between 2 migraine attacks and it may be due to endogenous or exogenous factors. In the few days preceding the next attack slow cortical potentials are highest and habituation delay experimentally recorded during contingent negative variation is at a maximum. These striking features of slow cortical potentials are predictors of the next attack. The pronounced negativity can be fed back to the patient. The data support the hypothesis that a change in amplitudes of slow cortical potentials is caused by altered habituation during the recording session. This kind of neurofeedback can be characterized as "empirically based" because it improves habituation and it proves to be clinically efficient.

Neuroreport 2002 Aug 7;13(11):1377-81  
**Functional MRI for neurofeedback: feasibility study on a hand motor task.**  
Yoo SS, Jolesz FA.  
Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis St, Boston, MA 02115, USA.  
We present an fMRI-based method that enables subjects to monitor and actively modulate their own brain activity as a form of biofeedback. On a 1.5 T clinical MR scanner, functional areas during a simple hand motor task were delineated by detecting signal variations associated with the brain activity. Then, the subject adopted a different strategy to expand the activation in motor and somatosensory areas that were not activated previously. Statistical maps of brain activity were visually presented back to the subject, being updated at the end of each segmented rest-task block in near real-time manner. Our results suggest that the visual feedback of the functional brain activation maps guided subjects to adjust their task performance to achieve the desired modulation of cortical activity. This method may offer a potential utility for fMRI-based neurofeedback.
The effect of training distinct neurofeedback protocols on aspects of cognitive performance

The results announced in the International Journal of Psychophysiology this month show a link between neurofeedback training and improved memory in a 40 person trial. More detail in the Imperial College London press release:

Http://www.ic.ac.uk/p3872.htm

Shaw, N.A.
The neurophysiology of concussion.
Progress in Neurobiology 67 (2002) 281-344

Cerebral concussion is both the most common and most puzzling type of traumatic brain injury (TBI). It is normally produced by acceleration (or deceleration) of the head and is characterized by a sudden brief impairment of consciousness, paralysis of reflex activity and loss of memory. It has long been acknowledged that one of the most worthwhile techniques for studying the acute pathophysiology of concussion is by the recording of neurophysiological activity such as the electroencephalogram (EEG) and sensory evoked potentials (EPs) from experimental animals. In the first parts of this review, the majority of such studies conducted during the past half century are critically reviewed. When potential methodological flaws and limitations such as anesthetic protocols, infliction of multiple blows and delay in onset of recordings were taken into account, two general principles could be adduced. First, the immediate post-concussive EEG was excitatory or epileptiform in nature. Second, the cortical EP waveform was totally lost during this period. In the second parts of this review, five theories of concussion which have been prominent during the past century are summarized and supportive evidence assessed. These are the vascular, reticular, centripetal, pontine cholinergic and convulsive hypotheses. It is concluded that only the convulsive theory is readily compatible with the neurophysiological data and can provide a totally viable explanation for concussion. The chief tenet of the convulsive theory is that since the symptoms of concussion bear a strong resemblance to those of a generalized epileptic seizure, then it is a reasonable assumption that similar pathobiological processes underlie them both. Further, it is demonstrated that EPs and EEGs recorded acutely following concussive trauma are indeed the same or similar to those obtained following the induction of a state of generalized seizure activity (GSA). According to the present incarnation of the convulsive theory, the energy imparted to the brain by the sudden mechanical loading of the head may generate turbulent rotatory and other movements of the cerebral hemispheres and so increase the chances of a tissue-deforming collision or impact between the cortex and the boney walls of the skull. In this conception, loss of consciousness is not orchestrated by disruption or interference with the function of the brainstem reticular activating system. Rather, it is due to functional deafferentation of the cortex as a consequence of diffuse mechanically-induced depolarization and synchronized discharge of cortical neurons. A convulsive theory can also explain traumatic amnesia, autonomic disturbances and the miscellaneous collection of symptoms of the post-concussion syndrome more adequately than any of its rivals. In addition, the symptoms of minor concussion (a.k.a. being stunned, dinged, or dazed) are often strikingly similar to minor
epilepsy such as petit mal. The relevance of the convulsive theory to a number of associated problems is also discussed. These include the relationship between concussion and more serious types of closed head injury, the utility of animal models of severe brain trauma, the etiology of the cognitive deficits which may linger long after a concussive injury, the use of concussive (captive bolt) techniques to stun farm animals prior to slaughter and the question of why some animals (such as the woodpecker) can tolerate massive accelerative forces without being knocked out.

*Memory test spots early Alzheimer's*


A verbal memory test is the best way of spotting the early stages of Alzheimer's diseases, experts believe.

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Courtesy of David Dillard
Temple University
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jwne@astro.temple.edu

These resources regarding a relationship between musculoskeletal disorders and smoking may be of interest to the members of this discussion group.

First a definition of musculoskeletal disorders:

Work-related Musculoskeletal Disorders,
Oregon, 1990-2000
by Mike Maier and Juli Ross-Mota
<http://www.cbs.state.or.us/external/imd/rasums/resalert/msd.html>

Musculoskeletal disorders are sometimes called ergonomic injuries and illnesses. Ergonomics is the study of the worker's interaction with tools, equipment, environment, jobs, tasks, work methods, work rates, and other systems. The federal Bureau of Labor Statistics (BLS) has defined musculoskeletal disorders (MSDs) as injuries and disorders to muscles, nerves, tendons, ligaments, joints, cartilage, and spinal discs. MSDs do not include injuries resulting from slips, trips, falls, or similar accidents. Examples of MSDs include many kinds of sprain and strain, carpal tunnel syndrome, tendinitis, sciatica, and low back pain. MSDs result from bodily reactions due to bending, climbing, crawling, reaching, or twisting, and from overexertion and repetitive motion. All statistics cited in this report are based on the BLS definition of MSDs.
OSHA has a repetitive strain injury information page that will provide a substantial body of information regarding the repetitive strain area of musculoskeletal disorders.

Repetitive Strain Injury (RSI)
<http://www.ohsu.edu/croet/injuries/strain.html>

> RSI Background info and resources
> Prevention and Treatment
> Exercises and Stretches
> Disorders Related to RSI
> Bursitis
> Carpal Tunnel
> Epicondylitis
> Tendonitis
> Trigger Finger

The above page provides a substantial body of useful links.

This page leads to more in depth information on Musculoskeletal Disorders (MSDs):

Musculoskeletal Disorders Clinical Resources
<http://fsumed-dl.slis.ua.edu/clinical/musculoskeletal/>

As does this page:

MUSCULOSKELETAL DISORDERS
<http://www.bioweb.uncc.edu/pathophys/musculos.htm>

With these background resources, here are some sources that consider the relationship between Musculoskeletal Disorders and smoking: Smoking Linked with Reports of Musculoskeletal Disorders A DGReview of: "Smoking and musculoskeletal disorders: findings from a British national survey." Annals of the Rheumatic Diseases (ARD Online) 12/27/2002
By Anne MacLennan

Link Reported Between Smoking and MSDs
January 20, 2003
from: Ergonomics Today

A recent study by researchers at the University of Southampton, England, suggests a possible
link between musculoskeletal disorders (MSDs) and cigarette smoking in both current and former smokers.

Published in the Annals of Rheumatic Diseases, the study of nearly 13,000 smoking and non-smoking respondents ages 16 to 64, looked at pain in the low back, neck, and upper and lower limbs during the preceding year. Questions were also asked regarding smoking habits, physical activities at work, headaches, tiredness and stress. The goal of the study was to determine whether or not a link existed between MSDs and cigarette smoking.

OSHA Postpones MSD Definition, Creates Alliance, and Announces Meeting Date for NACE

January 13, 2003

Smoking and musculoskeletal disorders: findings from a British national survey.
Source: Annals of the Rheumatic Diseases, 2002-12-27
Author: Palmer KT, Syddall H, Cooper C, Coggon D.
<http://www.tobacco.org/news/112549.html>

Intro: CONCLUSIONS: There is an association between smoking and report of regional pain, which is apparent even in ex-smokers. This could arise from a pharmacological effect of tobacco smoke (for example, on neurological processing of sensory information or nutrition of peripheral tissues); another possibility is that people with a low threshold for reporting pain and disability are more likely to take up and continue smoking.

Low-Back Musculoskeletal Disorders
<http://www.ergonext.com/aa-studies/studies-lowback.htm>

Back disorder is multifactorial in origin and may be associated with both occupational and nonwork-related factors and characteristics. The latter may include age, gender, cigarette smoking status, physical fitness level, anthropometric measures, lumbar mobility, strength, medical history, and structural abnormalities [Garg and Moore 1992].

Preventing Work-Related Musculoskeletal Disorders

A DoD information Guide for Supervisors and Workers
June 2000
<https://www.denix.osd.mil/denix/Public/Library/Ergonomics/Musculoskeletal/wmsd.html>
This guide is a product of the DoD Ergonomics Working Group
Visit their web site at

Preventing Low Back Pain.
Focus prevention on-

Reducing exposure to known risk factors such as repetition, awkward postures, or stress on muscles, tendons, joints, or the lower spine.

Conditioning or training the muscles to have a greater tolerance for physiological stress.

Losing weight. Extra pounds, especially around the middle, increase stress on the lower back.

Smoking cessation. Smoking can interfere with blood circulation to the lower back, and a constant cough can bring on a back spasm.

Exercising daily. Choose a sport that is easy on your back such as walking, swimming, or bicycling in an upright position.

________________________________________________________________________

REVIEW ARTICLE

Upper Extremity Musculoskeletal Disorders: Occupational Association and a Model for Prevention
John C. Rosecrance and Thomas M. Cook

Prevention of work related musculoskeletal disorders
http://www.arbo.nl/content/network/tnoarbeid/docs/musculoskeletal_proefschrift.pdf

Work factors and musculoskeletal disorders

http://www.sciencedaily.com/releases/2003/01/030124073832.htm - Study Shows How The Brain Pays Attention; Neural Circuits That Control Eye Movements Play Multiple Roles In Visual Attention

BTY, that news about NF and memory is now on science daily news as well -
http://www.sciencedaily.com/releases/2003/01/030123073326.htm - Researchers Find Link Between Improved Memory And The Use Of Neurofeedback

________________________________________________________________________
TO DO:

Ethics Chapter
BILLILNG
Sam: Goals and Delores Documentation
Bill CES and Computer (1200.00)
SARAH NOTES
ROZANC NOTES
ROZANC LETTER
SPOMER LETTER
JPTH Stuff
JCMC

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>From the Kaisernetwork.org

Sen. John Breaux (D-La.) on Jan. 23 will introduce a proposal that would achieve universal health care coverage by requiring all Americans to obtain private health insurance, USA Today reports. States would establish purchasing pools to ensure that people without employer-sponsored coverage could buy insurance at group rates (Welch, USA Today, 1/23). In addition, tax credits would be offered to help low- and middle-income U.S. residents purchase insurance (AP/Orlando Sentinel, 1/23). Federal subsidies would be available for the poor (USA Today, 1/23). The federal government would also establish individual health accounts for the poor, which could be used for physician copayments, premiums or other health expenses (AP/Orlando Sentinel, 1/23). Medicare would continue to provide care for people age 65 and older (USA Today, 1/23). Medicaid would continue in its current form for seniors, people with disabilities and long-term care patients, but low-income Medicaid beneficiaries would be covered under the new system (Breaux, Wall Street Journal, 1/23). Insurers would be barred from denying coverage to people with pre-existing conditions (AP/Orlando Sentinel, 1/23). A prescription drug benefit would be a part of all the policies. Breaux has not said how much the proposal would cost (USA Today, 1/23).

'New Social Contract'
The plan offered by Breaux, a moderate Democrat, is "an attempt to bridge ideological and partisan differences that have blocked health insurance reform" since former President Clinton's failed attempt in the early 1990s, according to USA Today (USA Today, 1/23). "The time has come to rethink our
health care system," Breaux writes in a Wall Street Journal opinion piece today. He continues, "Any new system must have at its core a new social contract that requires government and individuals to share equal responsibility for universal coverage," adding, "The solution is not a government-run system or a fend-for-yourself marketplace but, instead, a new approach that combines the best care options offered by the private sector backed by the resources and oversight of federal and state governments" (Wall Street Journal, 1/23). While the plan may not "provide a breakthrough" in this Congress, Breaux "hopes to push the issue to the top of the debate" for the 2004 presidential race and make universal health care, rather than a Medicare prescription drug benefit, the focal point of health policy debates, USA Today reports (USA Today, 1/23). Breaux will unveil the proposal in speeches at the National Health Policy Conference and before the U.S. Conference of Mayors (Orlando Sentinel, 1/22).

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Virginia Commonwealth Univ. Health Systems
Richmond, VA 23298-0661

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50 Natural Highs

Please make sure you forward this back to me -- you'll see why at the end! Think about them one at a time BEFORE going on to the next one....... IT DOES MAKE YOU FEEL GOOD, especially the thought at the end.

1. Falling in love.
2. Laughing so hard your face hurts.
3. A hot shower.
4. No lines at the supermarket
5. A special glance.
6. Getting mail
7. Taking a drive on a pretty road.
8. Hearing your favorite song on the radio.
9. Lying in bed listening to the rain outside.
10. Hot towels fresh out of the dryer.
11. Finding the sweater you want is on sale for half price.
12. Chocolate milkshake. (or vanilla!) (or strawberry)
15. Giggling.
16. A good conversation.
17. The beach
18. Finding a 20 note in your coat from last winter.
19. Laughing at yourself.
20. Midnight phone calls that last for hours.
21. Running through sprinklers.
22. Laughing for absolutely no reason at all.
23. Having someone tell you that you're beautiful.
24. Laughing at an inside joke.
25. Friends.
26. Accidentally overhearing someone say something nice about you.
27. Waking up and realizing you still have a few hours left to sleep.
28. Your first kiss (either the very first or with a new partner).
29. Making new friends or spending time with old ones.
31. Having someone play with your hair.
32. Sweet dreams.
33. Hot chocolate.
34. Road trips with friends.
35. Swinging on swings.
36. Wrapping presents under the Christmas tree while eating cookies and drinking your favorite tipple.
37. Song lyrics printed inside your new CD so you can sing along without feeling stupid.
38. Going to a really good concert.
39. Making eye contact with a cute stranger.
40. Winning a really competitive game.
41. Making chocolate chip cookies.
42. Having your friends send you homemade cookies.
43. Spending time with close friends.
44. Seeing smiles and hearing laughter from your friends.
45. Holding hands with someone you care about.
46. Running into an old friend and realizing that some things (good or bad) never change.
47. Riding the best roller coasters over and over.
48. Watching the expression on someone's face as they open a much desired present from you.
49. Watching the sunrise.
50. Getting out of bed every morning and being grateful for another beautiful day.

PASS ON THESE NATURAL HIGHS TO AT LEAST 7 PEOPLE IN THE NEXT HALF HOUR AND SOMETHING FANTASTIC WILL HAPPEN TO YOU IN THE NEXT FEW HOURS. Be sure to send it back to the person who sent it to you!

Friends are quiet angels who lift us to our feet when our wings have trouble remembering how to fly.
IME TALK

Physician Heal Thyself First
Secondary Gain does not just occur in patients....
Look at Kaiser Permanente
Decision Models based on restrictiveness of treatment delivery vs. restrictiveness of allowed nontreatment errors
We understand expectancy and bias in our patients (somatic vigilance) and the deleterious effects, but, what about the same in ourselves (i.e., malingering vigilance in context of reinforcement by payors to find it. Be the hero and find a malingerer. Become an insurance co. star and reinterpret your behavior as being objective...

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IME

Forensic Neuropsychology should not be the primary concern of the field of neuropsychology. Medicolegal arena represents, in many ways, the concentration of all that limits the field, while purporting to represent the highest level of scientific rigor:
1) one time exams with no opportunity for long term follow or collection of any program evaluation data;
2) offers the highest imbalance of record review to direct examinee time ration (see Cripe re: problems with overreliance on record reviews;
3) It is fraught with absence of objectivity data (e.g., objectivity ratios for degree of favorability of findings to referring party;
4) In an arena where money is driving most aspects of the situation, the focus is suspiciously vigilant to plaintiff secondary gain. Secondary losses are often minimized in defense reports. Secondary gain is vigilantly attended to in a way that parallels vigilance expectancy biases in plaintiff’s re: their symptoms, yet this is pretty much ignored (i.e., See what you look for, selective attention bias). Seoncary gain in IME’s is ignored
   (a) most NP’s spend more face to face time, and more time talking with Ref. Attorney than examineel;
   (b) If ratio of unfavorable (to ref. Side) findings is above small,
      i) future referrals are not made by attorney advocates;
      ii) NP gets unfavorably labelled in the attorney referral network and loses future referrals from attorney advocates;
(c) data from federal judges and attorneys working with medical experts show consistent findings of ratings of high and predominant expert bias non-objectivity;
(d) data from adjustors shows clear bias;
(e) data from survey (MFM) shows perception of greater insurance co and WC bias than injured worker bias;
(f) data from insurance companies (who pay for health care and are filthy rich (e.g., 47% profits in market where average = -10% last year) and evidence of bias is growing;
(g) restrictive insurance situations are clearly biasing / shaping prevailing opinions in the field...
Few findings of mixed or uncertain in FNP exams...does not reflect even distribution...
% of nonused is not that big

Focus on malingering and evidence of detection is not grounded in established data, and comparisons could be biased by erroneous assumptions and tautology.
Limitations of SVT’s were mentioned, and only 1, in about 10% of IME’s for defense, but over 50% in plaintiff generated IME’s.

Sweet paper: overrep of malingering...
Table 5: Diagnostic Realities in Assessment (e.g., ABI, Chronic Pain)

<table>
<thead>
<tr>
<th>Physical Disorder</th>
<th>Residual Functional Impairments</th>
<th>Residual Testing Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Yes</td>
<td>1. Yes, Not Exaggerated</td>
<td>1. Yes, Not Exaggerated</td>
</tr>
</tbody>
</table>

X = 4

Table 4: General Weaknesses of Symptom Validity Tests (SVT) / Measures

- 1) Psychometric Research Inadequacies: basic test construction issues such as reliability and validity.
- 2) Limited Generalizability of analogue research: unknown differences between simulated and real malingerers.
- 3) Variable Group Membership: wide variability in samples for both simulators and symptom / disorder groups.
- 4) Differential Vulnerability to Response Bias: some tests are more obvious while others are more subtle.
- 5) Questionable Generalizability of Findings: from one SVT to other tests, to actual symptoms, or across time.
- 6) Absence of Mutual Exclusivity: poor effort can occur in presence of real disorders.
- 7) Law of the Instrument: operational definitions wherein "malingering" becomes what malingering tests measure. Specifically, the definitions of "effort", and validation studies to examine the construct, are often missing. Further "effort" cannot be assumed uniform for mild TBI, chronic pain, and depression, and for nonlitigating and litigating situations.
- 8) Questionable Specificity: The effects of fatigue, pain, disinterest, non-attended (computer) administration, mixing cognitive tests and SVT's in a battery with unknown validity, and other factors on response bias tests, are not understood and have not been addressed.
- 9) Frequently High Misclassification (i.e., false positive or false negative) rates.
- 10) Use of most current SVT / Indexes with regard to diagnosis and decision making may violate APA ethics and "APA Standards for Educational and Psychological Tests", given the aforementioned psychometric limitations.

Table 2.
Primary Topics Covered In 337 Forensic Conference Presentations Abstracted in ACN, JCEN, and TCN from 1990 to 2000 (Based Only Upon Title and Abstract).

<table>
<thead>
<tr>
<th>Topic</th>
<th>Number of Presentations</th>
<th>% of All Forensic Presentations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malingering</td>
<td>242</td>
<td>72</td>
</tr>
<tr>
<td>Measures of Cognitive Abilities</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Measures of Personality/Emotion</td>
<td>21</td>
<td>6</td>
</tr>
<tr>
<td>Objective</td>
<td>20</td>
<td>95</td>
</tr>
<tr>
<td>Non-specific</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Projective</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pathology</td>
<td>13</td>
<td>4</td>
</tr>
</tbody>
</table>

Researchers and scholars assert that feigning should not be equated with malingering. Some practicing clinicians doing the everyday work of forensic assessment may view this as merely an academic distinction. This case study illustrates that a high level of certainty about feigning must not be considered indicative of malingering. The case also contrasts two models for assessing malingering and highlights the need for forensic examiners to present assessment-of-malingering data clearly and cautiously.

11 major health care insurers reported an average of 47% increase in profits in the 3rd quarter of 2002. 4th quarter profits are expected to be strong as well.

Premiums are expected to rise an average of 15.4%, with health costs increasing only 12% in 2003. This should provide another "good year" for insurers.

Meanwhile, 7.2 M Children remain uninsured and 39.4 M US residents under the age of 65 lack health care coverage.

Table 4. Specific Topics Covered in 139 Forensic Articles From 1990 Through 2000.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Number of Articles</th>
<th>% of All 139 Articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malingering</td>
<td>120</td>
<td>86</td>
</tr>
<tr>
<td>Measures of Cognitive Abilities</td>
<td>114</td>
<td>82</td>
</tr>
<tr>
<td>Decision Making</td>
<td>81</td>
<td>58</td>
</tr>
<tr>
<td>Psychometrics</td>
<td>55</td>
<td>40</td>
</tr>
<tr>
<td>Test Validity/Reliability</td>
<td>(50)</td>
<td>(36)</td>
</tr>
<tr>
<td>Litigation Effects</td>
<td>38</td>
<td>27</td>
</tr>
<tr>
<td>Base Rates</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>Ethics</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>Appropriate Tests</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>Expert Testimony</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Use of Norms</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Competency of Examinee</td>
<td>14</td>
<td>10</td>
</tr>
</tbody>
</table>
41.2 million uninsured in 2001
14.6% of citizens in 2001 (14.2% in 2000)
19.1 million children in 2001
15.5% of children (20.4% in 1997)

BMJ 2003;326:245 (1 February)
Detection of Alzheimer's disease and dementia in the preclinical phase: population based cohort study
Katie Palmer, PhD student, Lars Bäckman, professor, Bengt Winblad, professor, Laura Fratiglioni, professor.
Aging Research Center, Division of Geriatric Epidemiology and Medicine, Neurotec, Karolinska Institute, and Stockholm Gerontology Research Center, Box 6401, 11382, Stockholm, Sweden
Correspondence to: K Palmer katie.palmer@neurotec.ki.se
Objectives: To evaluate a simple three step procedure to identify people in the general population who are in the preclinical phase of Alzheimer's disease and dementia.
Design: Three year population based cohort study.
Setting: Kungsholmen cohort, Stockholm, Sweden.
Participants: 1435 people aged 75-95 years without dementia.
Assessments: Single question asking about memory complaints, assessment by mini-mental state examination, and neuropsychological testing.
Main outcome measure: Alzheimer's disease and dementia at three year follow up.
Results: None of the three instruments was sufficiently predictive of Alzheimer's disease and dementia when administered separately. After participants had been screened for memory complaints and global cognitive impairment, specific tests of word recall and verbal fluency had positive predictive values for dementia of 85-100% (95% confidence intervals range from 62% to 100%). However, only 18% of future dementia cases were identified in the preclinical phase by this three step procedure. Memory complaints were the most sensitive indicator of Alzheimer's disease and dementia in the whole population, but only half the future dementia cases reported memory problems three years before diagnosis.
Conclusion: This three step procedure, which simulates what might occur in clinical practice, has a high positive predictive value for dementia, although only a small number of future cases can be identified.

Proc Natl Acad Sci U S A 2003 Jan 24; [epub ahead of print]
Course of illness, hippocampal function, and hippocampal volume in major depression.
MacQueen GM, Campbell S, McEwen BS, Macdonald K, Amano S, Joffe RT, Nahmias C, Young LT.
Studies have examined hippocampal function and volume in depressed subjects, but none have systematically compared never-treated first-episode patients with those who have had multiple episodes. We sought to compare hippocampal function, as assessed by performance on hippocampal-dependent recollection memory tests, and hippocampal volumes, as measured in a 1.5-T magnetic resonance imager, in depressed subjects experiencing a postpubertal onset of depression. Twenty never-treated depressed subjects in a first episode of depression were compared with matched healthy control subjects. Seventeen depressed subjects with multiple past episodes of depression were also compared with matched healthy controls and to the first-episode patients. Both first- and multiple-episode depressed groups had hippocampal dysfunction apparent on several tests of recollection memory; only depressed subjects with multiple depressive episodes had hippocampal volume reductions. Curve-fitting analysis revealed a significant logarithmic association between illness duration and hippocampal volume. Reductions in hippocampal volume may not antedate illness onset, but volume may decrease at the greatest rate in the early years after illness onset.

Driving Ability Under Long-Term Treatment with Transdermal Fentanyl
Rainer Sabatowski, MD, Susanne Schwalen, MD, Klaus Rettig, MS, Klaus W. Herberg, MD, Stephan M. Kasper, MD, and Lukas Radbruch, MD

Clinical experience shows that neuropsychological side effects due to opioid therapy usually decrease during the first weeks of therapy. However, the effect of long-term treatment with transdermal fentanyl on complex activities, such as driving, is not yet clear. In a prospective trial, patients with continuous noncancer pain, who had received stable doses of transdermal fentanyl for at least 2 weeks, completed a series of computerized tests to measure attention, reaction, visual orientation, motor coordination and vigilance. Data from 90 healthy volunteers were matched to 30 patients; 9 patients were excluded from the per-protocol analysis because they took additional drugs in violation of the protocol. None of the performance measures for the 21 remaining fentanyl patients was significantly inferior to the controls. We conclude that stable doses of transdermal fentanyl for the treatment of chronic non-cancer pain are not associated with significant impairments in psychomotor and cognitive performance. The threshold for fitness to drive as defined by German law did not differ significantly between the groups.

Psychopharmacol Bull 2002 Summer;36 Suppl 2:158-65

Can we distinguish anxiety from depression?
Baldwin DS, Evans DL, Hirschfeld RM, Kasper S.
Department of Psychiatry, University of Southampton, Hampshire, United Kingdom.
dsb1@soton.ac.uk

It is becoming increasingly apparent that although anxiety and depression are separate syndromes and can be identified as such, there is considerable overlap of clinical symptoms and pathophysiological processes. Data indicate that comorbid anxiety and depression is more common than either disorder alone. A large US study found that 58% of individuals with a history of depression also had an anxiety disorder, and a study by the World Health Organization showed that anxiety and depression were the most common coexisting psychological problems in primary care. Generalized anxiety disorder in particular is strongly comorbid with, and commonly precedes, major depression. The implications of comorbid anxiety and depression are
significant, with increased social and psychological impairment, and poorer clinical outcomes and prognosis. Anxiety and depression coexist at much higher rates than would be expected by chance alone, suggesting that the two disorders are closely related and may have a common cause. Disturbances of serotonin and norepinephrine neurotransmission are both implicated in anxiety and depression, and new evidence suggests that these systems may provide a mechanistic link between the two disorders, with changes in one system being reflected in the other. Abnormal homeostasis of these two systems may result in anxiety and depression. New theories hypothesize a continuum of illness, with anxiety and depression possibly being different phenotypic expressions of a common neurobiological origin. There is still uncertainty regarding the neurobiological cause, but it is probably linked to dysregulation in the serotonergic and noradrenergic systems.

Comment in:

Effects of methylphenidate discontinuation on cerebral blood flow in prepubescent boys with attention deficit hyperactivity disorder.
Langleben DD, Acton PD, Austin G, Elman I, Krikorian G, Monterosso JR, Portnoy O, Ridlehuber HW, Strauss HW.
Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA. langlebe@mail.med.upenn.edu

Methylphenidate (MPH) is an effective symptomatic treatment of attention deficit hyperactivity disorder (ADHD), but the mechanisms of its therapeutic action have not been fully elucidated. To address this issue, we assessed the effects of discontinuation of chronic MPH treatment on regional cerebral blood flow (rCBF) in ADHD patients. METHODS: Twenty-two prepubescent boys with ADHD (age range, 8.2-11.5 y) and 7 healthy volunteers were studied with SPECT on and off MPH. Their rCBF data were automatically normalized to whole-brain counts and coregistered with standard anatomic space. rCBF changes were evaluated with statistical parametric mapping based on voxel-by-voxel ANOVA. RESULTS: When the subjects were not taking MPH, rCBF was higher in the motor, premotor, and the anterior cingulate cortices (Brodmann's areas 4, 6, and 32). CONCLUSION: Brief discontinuation of MPH treatment is associated with increased motor and anterior cingulate cortical activity. Our findings suggest that MPH treatment modulates motor and anterior cingulate cortical activity directly or indirectly. Alternatively, our findings may be related to MPH withdrawal. These data provide novel information on the potential mechanisms of the therapeutic action of MPH. Furthermore, they are clinically relevant to the commonly occurring brief interruptions in MPH treatment.

NeuroRehabilitation 2002;17(4):333-44

Executive dysfunction following traumatic brain injury: Neural substrates and treatment strategies.
McAllister TW, McDonald BC, Flashman LA, Saykin AJ.
Executive dysfunction is among the most common and disabling aspects of cognitive impairment following traumatic brain injury (TBI), and may include deficits in reasoning, planning, concept formation, mental flexibility, aspects of attention and awareness, and purposeful behavior. These impairments are generally attributed to frontal systems dysfunction, due either to direct insult to the frontal lobes or to disruption of their connections to other brain regions. Evaluation of executive deficits typically includes neuropsychological assessment, though adjunctive interviews can be critical in detecting subtle dysexecutive symptoms that may not be apparent on standardized testing. Rehabilitation programs emphasizing cognitive-behavioral approaches to the retraining of planning and problem-solving skills can be effective in ameliorating identified executive deficits. In addition, pharmacological approaches may be useful in addressing aspects of executive dysfunction. This review summarizes the nature of executive deficits following TBI, their neuroanatomical substrates, selected assessment and treatment strategies, and recent research findings and trends.


A large body of evidence indicates that people attribute unwarranted causality (influence) to a stimulus simply because it is more noticeable or salient than other available stimuli. This article reviews recent research demonstrating that this illusory-causation phenomenon can produce serious prejudicial effects with regard to how people evaluate certain types of evidence. Specifically, evaluations of videotaped confessions can be significantly altered by presumably inconsequential changes in the camera perspective taken when the confessions are initially recorded. Videotaped confessions recorded with the camera focused on the suspect -- compared with videotapes from other camera points of view (e.g., focused equally on the suspect and interrogator) or with more traditional presentation formats (i.e., transcripts and audiotapes) -- lead mock jurors to judge that the confessions were more voluntary and, most important, that the suspects are more likely to be guilty. Because actual criminal interrogations are customarily videotaped with the camera lens zeroed in on the suspect, these findings are of considerable practical significance.

http://www.appliedneuroscience.com/gpage4.html
2.1, January 29, 2003
Robert W. Thatcher, Ph.D., 1,2, Carl J. Biver, Ph.D. 1 and Duane North, M.S. 1
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Abstract
16- *L”L”Hz 0††ˆŒ &† ™ ☺†P”Lˆ, 522 U.S. 136 113 S.Ct. 2786, 125 L.Ed.2d 469 (1997).


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Statistical Focus: Misuses of Statistics in Govt, Media and Science...

http://www.stats.org/

Study: Review in AMA Journal by 2 Yale Univ researchers found ¼ of univ-based med researchers receive funding from drug cos, ties that can distort the study. Reports suggest that industry may alter, obstruct or even stop publication of negative studies.

Wall Street Journal, Associated Press 01/22/2003

Beth
Fax: 757-356-0287
Phone 757-356-9076

Dan Hall
901-6301
Good mechanic, but no driver’s license

Dana Hamel
Chronic Pain

2.5 years post abdominal resection surgery, two adhesion operations. He is an aviator and has been treated at John Hopkins, where they want to give antidepressants, and this would void his license.

Lives in Richmond. International aviator.

Hopkins, tried injection, without help, from Neurolgist, Melika.

Sunday, 2pm, dark and inactive in apt when sister visited

Noone knew where his cane was, or even seemed concerned initially that they didn’t

TV on and watching staff interest program, and loudly discussing, when Fred was disintereted and not included.

Sheila’s Assessment:
1) Therapeutic Assignments and activities
2) Competency in carrying out therapeutic activities
3) General therapeutic interactional competency

RX:
Staff training...

Schedule:
Grocery store outing with assignment to:
1) choose a desired item (e.g., popcorn, baked cookie role);
2) problem solve how to find the item in the store;
3) return and include, using continuing Method of Vanishing Cues, cooking, subsequent dishwashing, etc.

Overall Client Goal Structure
Scheduled Activities
LST Neurobehavioral Therapist Goal Directed Activity Expectation
LST Job descriptions
Add: Conduct TX activities consistent with individualized, and general client goals, in individual and group formats.

Super X5DA8, Dual Socket 604 for Xeon 533/400, 0/12GB DDR, 6x184-pin DIMM, Intel E7505 chipset, 8X AGP Pro 1.5V, 1x133MHz, 2x100MHz PCI-X, 2x32-bit PCI, Adaptec 2-CH Ultra320 SCSI, Intel 82545EM Gigabit LAN, 6-CH Audio, Ext. ATX - Motherboard only
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============================================================================

Kjaergard LL, Als-Nielsen B.
Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the BMJ.
BMJ 2002 Aug 3;325(7358):249

OBJECTIVE: To assess the association between competing interests and authors' conclusions in randomised clinical trials. DESIGN: Epidemiological study of randomised clinical trials published in the BMJ from January 1997 to June 2001. Financial competing interests were defined as funding by for profit organisations and other competing interests as personal, academic, or political. Studies: 159 trials from 12 medical specialties. MAIN OUTCOME MEASURES: Authors' conclusions defined as interpretation of extent to which overall results favoured experimental intervention. Conclusions appraised on 6 point scale; higher scores favour experimental intervention. RESULTS: Authors' conclusions were significantly more positive towards the experimental intervention in trials funded by for profit organisations alone compared with trials without competing interests (mean difference 0.48 (SE 0.13), P=0.014), trials funded by both for profit and non-profit organisations (0.30 (SE 0.10), P=0.003!), and trials with other competing interests (0.45 (SE 0.13), P=0.006). Other competing interests and funding from both for profit and non-profit organisations were not significantly associated with authors' conclusions. The association between financial competing interests and authors' conclusions was not explained by methodological quality, statistical power, type of experimental intervention (pharmacological or non-pharmacological), type of control intervention (for example, placebo or active drug), or medical specialty. CONCLUSIONS: Authors' conclusions in randomised clinical trials significantly favoured experimental interventions if financial
competing interests were declared. Other competing interests were not significantly associated with authors' conclusions.

The Relationship of Neck Injury and Post-traumatic Headache
Russell C Packard MD

Although there may be several causes of post-traumatic headache, neck injury is perhaps the most common. This paper primarily reviews the relationship of neck injury, whiplash, and post-traumatic headache. Mechanisms may include structural damage from acceleration or extension of the neck, development of myofascial pain and trigger points, interaction of the trigeminal nociceptive system with the upper cervical (occipital) nerves, and psychologic and emotional factors. Although some healing will occur, the outcome may depend on a number of human factors (awareness of an impending collision) and the fact that repaired tissue is different from normal, uninjured tissue.

DIPLOMA MILLS

General information about diploma mills:
http://www.degreefinders.com/diplomamills.html

Information on the "Top Ten" (twelve) diploma mills:

A website with multiple links concerning diploma mills:
http://www.web-miner.com/deunaccredited.htm

A website describing a cat obtaining credentials:
http://users.snip.net/~drsteve/Articles/Dr_Zoe.htm

Top 12 Diploma Mills
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2. La Salle University (Louisiana)
3. Chadwick University (Alabama)
4. American State University (Hawaii)
5. American International University (Alabama)
6. Columbus University (Louisiana)
7. Monticello University (Kansas)
8. Frederick Taylor University (California)
9. Pacific Western University (Hawaii)
10. City University (California)
11. Kennedy Western University (Hawaii)
12. Trinity University (Great Britain)

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Messages:

Jessica Reach, 3rd year counseling...summer practicum. Expectations and assessment and therapy opportunities.  358-8118

Braxton from Calgary....
403-701-8788

Jane Brittingham...
323-4108

Renee Bernardo, now supposedly authorized...
754-1394

JoAnn R: Computer...

BILLING

JHTR

IJFP Paper
Alvin Lake in Michigan, who has PTHA data. and Russell Packard, MDDir., H/a Mgt. and Neurology Professor of Psychology/Psychiatry University of West Florida Pensacola, F

Alvin E. Lake III, Ph.D.
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Alvin E. Lake III, Ph.D.

Director of the Behavioral Medicine Division at the Institute. Dr. Lake is a licensed psychologist and is considered an authority on psychological aspects of headache. He has achieved national recognition for his clinical work, educational programs, and research in headache. Dr. Lake is on the editorial board of the journal Headache, an invited lecturer to audiences throughout the nation, and an active committee member in the American Association for the Study of Headache. Currently the President of the Michigan Society for Behavioral Medicine and Biofeedback, Dr. Lake is a nationally certified biofeedback practitioner (B.C.I.A.). He is Associate Director of the Head Pain Treatment Unit at Chelsea Community Hospital. Dr. Lake received his Ph.D. from the University of Michigan and has written extensively on biofeedback and head pain. He is a founding member of the Institute and has been an influential force in its direction and accomplishments since 1978.

Large-scale surveys are being performed to detail the impact of headache and pain on individuals, their families, employers, and society at large. Studies on prevalence, effect on quality of life, loss of work time, and health care costs associated with pain are underway.

Consistent with its mission, MHNI is actively involved in a wide range of clinical research projects. These include studies on investigational medications, important clinical phenomena in headache and pain conditions, and better ways to assess and evaluate patients in pain. Participants in research projects come from MHNI's own population of patients, through referral from community physicians, and include individuals who have referred themselves.

Interested in PTHA...

Russell Packard, MDDir., H/a Mgt. and Neurology Professor of Psychology/Psychiatry University of West Florida Pensacola

EEG Biofeedback...
Russell C Packard MD

The Relationship of Neck Injury and Post-traumatic Headache

Although there may be several causes of post-traumatic headache, neck injury is perhaps the most common. This paper primarily reviews the relationship of neck injury, whiplash, and post-traumatic headache. Mechanisms may include structural damage from acceleration or extension of the neck, development of myofascial pain and trigger points, interaction of the trigeminal nociceptive system with the upper cervical (occipital) nerves, and psychologic and emotional factors. Although some healing will occur, the outcome may depend on a number of human factors (awareness of an impending collision) and the fact that repaired tissue is different from normal, uninjured tissue.

Anticonvulsants for the Treatment of Neuropathic Pain Syndromes
Miroslav Backonja MD
Department of Neurology H6570, 600 Highland Avenue, University of Wisconsin Hospital, Madison, WI, 53792, USA

This article is an evidence-based summary of randomized clinical trials published in peer-reviewed journals regarding the efficacy of anticonvulsants for the treatment of neuropathic pain.

Antidepressants in the Treatment of Migraine Headache
Nestor C Punay MD and James R Couch MD PhD
Department of Neurology, 711 SL Young Boulevard, The University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA

Antidepressants, particularly tricyclic antidepressants, have been a mainstay in the prophylactic therapy of migraine. The tricyclic antidepressants amitriptyline, nortriptyline, and doxepin have been the major agents for prophylactic treatment of migraine. These cause significant side effects in some patients. The high-affinity selective serotonin reuptake inhibitors and other newer antidepressants have been disappointing and much less effective in the treatment of migraine. In patients who are depressed with severe migraine, a tricyclic antidepressant may treat both conditions; however, the addition of a newer atypical antidepressant may be needed.

Borderline personality disorder and the chronic headache patient: Review and management recommendations
Saper, Joel R; Lake, Alvin E 33

Discusses the management of headache suffered by individuals with borderline personality disorder (BPD). BPD occurs in approximately 2% of the general population, with increased prevalence in patients with comorbid psychopathology and substance abuse. Severe headaches and migraine appear to be more prevalent in BPD patients than the general
population. A reported history of abuse is common, but must be interpreted with caution. Recent research has found reduced hippocampal volume in female BPD patients; hypometabolism in the premotor, prefrontal, and anterior cingulate cortex, and the thalamic, caudate, and lenticular nuclei; and serotonergic dysfunction. Opioid medications may adversely affect certain clinical features of BPD. Some BPD patients show at least short-term improvement in dissociative behavior when given opioid antagonists. Treatment should combine appropriate pharmacotherapy with ongoing psychotherapy. Early identification of BPD is likely to improve the course of treatment. Treatment often requires explicit contracts, consistent limit setting, confrontation, and communication between different treating professionals. The recognition and management of the physician's own countertransference is important to successful management.

Assessment and psychological management of recurrent headache disorders
Holroyd, Kenneth A
This article updates earlier reviews of recurrent headache disorders published in 1982 and 1992, selectively reviewing research published since 1990. Current issues in assessment (headache diagnosis, psychophysiology, comorbid psychopathology, quality-of-life assessment, and new assessment technologies) and psychological treatment (efficacy, therapeutic mechanisms, treatment delivery, and integration with drug therapy) are addressed. The author emphasizes the need to adapt psychological treatments to the severity of the headache disorder and to developments in drug therapy. Opportunities for the integration of biological, medical, and psychological science are highlighted.

Behavioral management of recurrent headache: Three decades of experience and empiricism
Penzien, Donald B; Rains, Jeanetta C; Andrasik, Frank
In the past 3 decades, behavioral interventions (BIs; chiefly relaxation, biofeedback, and stress-management) have become standard components of the armamentarium for management of migraine and tension-type headaches. Meta-analytic literature reviews of these BIs have consistently identified clinically significant reductions in recurrent headache. Across studies, BIs have yielded approximately 35-50% reduction in migraine and tension-type headache activity. Although we have only recently begun to directly compare standard drug and nondrug treatments for headache, the available evidence suggests that the level of headache improvement with BIs may rival those obtained with widely used pharmacologic therapies in representative patient samples. In recent years, some attempts have been made to increase the availability and cost effectiveness of BIs through alternative delivery formats and mass communications. Recent developments within diagnosis and classification are summarized, pointing out implication for behavioral researchers. Select future directions are discussed, which
include impact of the triptans, cost and cost effectiveness, and integration of behavioral treatments into primary care settings, the place where the great majority of headache sufferers receive treatment.

**Chronic daily headaches: A clinician's perspective**
Saper, Joel R
Headache. Vol 42(6), Jun 2002, pp. 538-542

The author outlines his perspectives as a clinician on a syndrome he named chronic headache complex, also called transformational migraine, and his evolving beliefs regarding the origins of chronic daily headache (CDH). He concludes that CDH is in most instances a progressive form of a primary disorder, most notably migraine. It is likely to be genetically influenced, if not determined, but many variables may augment and enhance the progression. Genetic determinants also may influence key physiological thresholds, including responsiveness to emotional duress or medication overuse and to pain itself. Once activated, a progressive process, perhaps fed by a disordered psychophysiological environment, promotes the development of the self-sustaining and escalating phenomenon of CDH. Early, if not pre-emptive, intervention thus may be critical and must include the elimination of any offending processes. Pharmacotherapy must be creative and at times aggressive and should be administered in conjunction with comprehensive care services, including those that assist in restoring healthier mind and body environments. Finally, J. Olesen's work is cited regarding the role of myofascial, supratentorial, or cervical influences in targeting brainstem mechanisms and thus provoking headache.

Related Articles, Links

**Effects of stimulant medications on the EEG of children with Attention-Deficit/Hyperactivity Disorder Predominantly Inattentive type.**
Clarke AR, Barry RJ, McCarthy R, Selikowitz M, Brown CR, Croft RJ.
Brain & Behaviour Research Institute and Department of Psychology, University of Wollongong, 2522, Wollongong, Australia

Stimulant medications are the most commonly-used treatments for Attention-Deficit/Hyperactivity Disorder (ADHD) in North America and Australia, although it is still not entirely known how these medications work. This study investigated the effects of stimulant medications on the EEG of children with the Inattentive type of ADHD. An initial EEG was recorded during an eyes-closed resting condition and Fourier transformed to provide absolute and relative power estimates for the delta, theta, alpha and beta bands. Theta/alpha and theta/beta ratios were also calculated. Subjects were placed on a 6-month trial of a stimulant and a second EEG was recorded at the end of the trial. Subjects were included in this study only if they showed a good clinical response during the trial. The unmedicated ADHD group had significantly greater absolute and relative theta, less relative alpha, and higher theta/alpha and theta/beta ratios than the control group. **The stimulant medications resulted in a**
normalisation of the EEG, with changes in the theta, alpha and beta bands being most evident. These results suggest that stimulants act to increase cortical arousal in children with ADHD, normalising their EEG.


Social Skills Training in Children With Attention Deficit Hyperactivity Disorder: A Randomized-Controlled Clinical Trial.
Antshel KM, Remer R.
Children's Hospital-Boston University of Kentucky. Antshelk@upstate.edu
Evaluated efficacy of social skills training (SST) on children with 2 subtypes of attention deficit hyperactivity disorder (ADHD). Participants were 120 children (30 girls, 90 boys), ages 8 to 12 with ADHD-Inattentive type (ADHD-I; n = 59) or Combined type (ADHD-C; n = 61). The children were randomly assigned within diagnosis subtype to the treatment condition (8 weeks of SST) or the no-intervention control condition. SST led to greater improvements in both parent- and child-perceived assertion skills in the children with ADHD, yet did not affect the other domains of social competence. Diagnostically heterogeneous groups led to greater improvements on parent-report of their child's cooperation and assertion abilities as well as children's report of their own empathy skills. Diagnostically homogeneous groups led to greater decreases in externalizing behaviors at posttreatment but not at follow-up. Children with comorbid oppositional defiant disorder (ODD) did not benefit as much from the intervention. Children with ADHD-I improved in assertion skills more than children with ADHD-C, yet the 2 diagnostic entities did not differ in improvement levels across all other social skills.


This study investigated the effects of seizure laterality and language dominance on material-specific memory in temporal lobe epilepsy (TLE). Left TLE (LTLE) patients with left-hemisphere language dominance (LHLD) showed significantly higher nonverbal than verbal memory capacity, whereas right TLE patients with LHLD showed significantly better verbal than nonverbal memory capacity. LTLE patients with non-left-hemisphere language dominance (NLHLD) showed significantly better verbal memory capacity compared with LTLE patients with LHLD. Thus, selective verbal or nonverbal memory deficits that are dependent on side of seizure onset were apparent in patients with LHLD but not in patients with NLHLD. Relative sparing of verbal memory capacity in LTLE patients with NLHLD may reflect interhemispheric reorganization of verbal memory function.
Seizure 2003 Mar;12(2):121-125
Risk factors and outcome of mood disorders in epilepsy: a case-control study.
JAGADHEESAN K, GARG AK, NIZAMIE SH.
Central Institute of Psychiatry, Kanke (PO), -834006, Ranchi, India

BACKGROUND: This case-control study investigated both the risk factors and outcome of mood disorders in epilepsy.

METHODS: For this study, 44 patients with both epilepsy and a mood disorder (study group) were compared with 44 randomly selected patients of epilepsy without a mood disorder (control group). Psychiatric diagnosis was made as per ICD-10 Diagnostic Criteria for Research (ICD-10 DCR). International classification for seizure types (1981) was used for classification of seizure types.

RESULTS: Of the patients in the study group, a majority were educated up to at least primary level, had later onset of seizures, longer duration of epilepsy and cluster attacks. The outcome of mood disorders in epilepsy was found good in most.

CONCLUSIONS: Educated patients who develop epilepsy at a later age and patients with poorly controlled epilepsy are more likely to experience mood disorders. In most patients with epilepsy, mood disorders remit completely; notably, in some patients affective symptoms resolve spontaneously.

Epileptic seizures are preceded by a decrease in synchronization.
Mormann F, Kreuz T, Andrzejak RG, David P, Lehnertz K, Elger CE.
Department of Epileptology, University of Bonn, Sigmund-Freud-Strasse 25, 53105, Bonn, Germany

The exact mechanisms leading to the occurrence of epileptic seizures in humans are still poorly understood. It is widely accepted, however, that the process of seizure generation is closely associated with an abnormal synchronization of neurons. In order to investigate this process, we here measure phase synchronization between different regions of the brain using intracranial EEG recordings. Based on our preliminary finding of a preictal drop in synchronization, we investigate whether this phenomenon can be used as a sensitive and specific criterion to characterize a preseizure state and to distinguish this state from the interictal interval.

Applying an automated technique for detecting decreased synchronization to EEG recordings from a group of 18 patients with focal epilepsy comprising a total of 117h, we observe a characteristic decrease in synchronization prior to 26 out of 32 analyzed seizures at a very high specificity as tested on interictal recordings. The duration of this preictal state is found to range from several minutes up to a few hours. Investigation of the spatial distribution of preictal desynchronization indicates that the process of seizure generation in focal epilepsy is not necessarily confined to the focus itself but may instead involve more distant, even contralateral areas of the brain. Finally, we demonstrate an intrahemispheric asymmetry in the spatial dynamics of preictal desynchronization that is found in the majority of seizures and appears to be an immanent part of the mechanisms underlying the initiation of seizures in humans.
Amygdala Kindling in Proechimys guyannensis Rat: An Animal Model of Resistance to Epilepsy.
De Amorim Carvalho R, Arida RM, Cavalheiro EA.
Laboratorio de Neurologia Experimental, Universidade Federal de Sao Paulo, Escola Paulista de Medicina, Sao Paulo, Brasil.
PURPOSE: This study examined the effect of amygdala kindling development in Proechimys guyannensis rat, a common rodent of the Amazon basin. METHODS: Adult male P. guyannensis animals (n = 43) and adult male Wistar rats (n = 14) were submitted to electrical amygdala kindling. RESULTS: From 43 Proechimys rats submitted to the kindling process, only three animals reached stage 5 of kindling. During the kindling development (stages 4-5), these animals had behavioral alterations different from those observed in Wistar rats. A longer time spent in stages 1-3 and 5 and longer afterdischarge duration in stages 1-4 was observed in the Proechimys group compared with the Wistar group. The number of wet-dog shakes also was reduced in the Proechimys group during the kindling process. CONCLUSIONS: These findings suggest natural endogenous inhibitory mechanisms in this animal species.

Cognitive retraining in epilepsy.
Gupta A, Naorem T.
Department of Psychology, University of Delhi, Delhi-110 007, India.
Epilepsy is the commonest neurological disorder, so there is a need to establish more effective remedial programmes for the deficits in cognitive functioning associated with epilepsy. The present paper studies the relative change in the targeted skill areas as a consequence of cognitive retraining. For this purpose, a pre- and post-multiple baseline design was adopted with the intention of treating specific deficient skill. The measures of neuropsychological functioning adopted were a composite of tests/tasks, with specific emphasis on attention, memory and emotional status. The subject was targeted to a special neuro-rehabilitation programme comprised of cognitive retraining, supportive therapy and a deep breathing relaxation exercise. A regular home intervention programme was conducted simultaneously. Cognitive retraining included both paper and pencil tasks and real life activities. The training programme covered a 6-week period and each weekly session lasted approximately 1 hour. The results showed an overall improvement in cognitive performance across sessions, and the regular home intervention sessions were found to have enhanced the subject's performance. In conclusion, it was noted that by identifying cognitive deficits, effective training programmes can be devised that will be of substantial benefit to patients with epilepsy.

CNS Drugs 2003;17(2):101-15
Vagal nerve stimulation (VNS) for the treatment of refractory epilepsy appears to have started from the theory that since VNS can alter the EEG, it may influence epilepsy. It proved effective in several models of epilepsy and was then tried in short-term, open-label and double-blind trials, leading to approval in Canada, Europe and the US. Follow-up observations in these patients demonstrated continued improvement in seizure control for up to 2 years. Close to 50% of treated patients have achieved at least a 50% reduction in seizure frequency. This therapy was also useful as rescue therapy for ongoing seizures in some patients; many patients are more alert. The initial trials were completed in patients >/=12 years of age with refractory partial seizures. Subsequently, similar benefits were shown in patients with tuberous sclerosis complex, Lennox-Gastaut syndrome, hypothalamic hamartomas and primary generalised seizures. Implanting the generator and leads is technically easy, and complications are few. The method of action is largely unknown, although VNS appears to alter metabolic activity in specific brain nuclei. Considering that improvement in mood is frequently found in patients using VNS, it has undergone trials in patients with depression. Other illnesses deserving exploration with this unusual therapy are Alzheimer's disease and autism. Some aspects of VNS have proven disappointing. Although patients have fewer seizures, the number of antiepileptic drugs they take is not significantly reduced. In addition, there is no way to accurately predict the end of life of the generator. Optimal stimulation parameters, if they exist, are unknown. Deep brain stimulation is a new method for controlling medically refractory seizures. It is based on the observation that thalamic stimulation can influence the EEG over a wide area. Several thalamic nuclei have been the object of stimulation in different groups of patients. Intraoperative brain imaging is essential for electrode placement. The procedure is done under local anaesthesia. Experience with this therapy is currently limited, but growing.
and they feel that the epilepsy is accepted in society. Restrictions are limited to activities such as swimming. Consequently, quality of life (QOL) is high for the majority of the patients, with only 6% of the patients reporting a low QOL.

**DISCUSSION:** It is often claimed that people with epilepsy, as a group, have more psychosocial problems than control populations of healthy subjects. As this may be true for the average comparisons between patients with epilepsy and controls, we must take into account during clinical practice that these problems occur predominantly in the minority of patients with refractory epilepsy. Patients with well-controlled epilepsy do not show worrying reactions to the epilepsy.

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**Epilepsia** 2003 Jan;44 Suppl 1:21-4

*Neuropsychiatric disorders in epilepsy: some transcultural issues.*

Trimble MR, Krishnamoorthy ES.

Department of Behavioural Neurology, Institute of Neurology, London, United Kingdom; and Research Department, National Neuroscience Institute, Singapore.

**PURPOSE:** To review transcultural perspectives in the neuropsychiatry of epilepsy. **METHODS:** Systematic literature searches of standard databases, cross-referencing, chapters, and opinion leader articles. **RESULTS:** Articles from the Indian subcontinent, Africa, and Japan were identified and are reviewed herein. The spectrum of psychopathology in epilepsy is rather similar across cultures. However, psychopathology specific to epilepsy, the interictal behavioural syndrome of Geschwind, for example, has not been well studied outside the Western world. Discussion: There is a need for well-designed epidemiological studies of neuropsychiatric disorders in epilepsy. These should use harmonised protocols and outcome measures. Special attention should be paid to the impact of aetiology on psychiatric co-morbidity and disablement.

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**Seizure** 2003 Mar;12(2):110-114

*Epilepsy in children with cerebral palsy.*

GURURAJ AK, SZTRIHA L, BENER A, DAWODU A, EAPEN V V.

Department of Paediatrics, Faculty of Medicine, UAE University, PO Box 17666, Al Ain, United Arab Emirates

**OBJECTIVES:** To study the occurrence, associated factors, nature and prognosis of seizures in children with cerebral palsy (CP). **DESIGN:** A prospective, descriptive, hospital-based, case-control study. **SETTING:** Tertiary level University Teaching Hospitals in the Al Ain Medical District, United Arab Emirates. **PATIENTS:** Fifty-six children with CP and seizures seen in the neurodevelopmental clinics at Al Ain and Tawam University Hospitals during the period of 1997-1999 were studied (group 1). Two control groups of 35 children with CP without seizures (group 2) and 50 children with seizures but no CP (group 3) were also studied. **RESULTS:** Spastic tetraplegia was the commonest type of CP associated with seizures whereas spastic diplegia was the commonest variety of CP in group 2. Most children with CP had an early onset of seizures within the first year of life as against those without CP. The children in group 1 had a higher incidence of neonatal seizures (42.9% vs. 29.4% in group 2 and 0% in group 3), presence of significant developmental delay (98.2% vs. 20.0% in group 3), occurrence of significant abnormalities on brain imaging (94.6% vs. 19.6% in group 3) and a need for use of more than 1 antiepileptic drug (66.1% vs. 30.0% in group 3). Over half of children in the study group
presented with generalized tonic clonic seizures; the electroencephalogram (EEG) showed focal epileptic discharges with or without secondary generalization in 39.3%. The overall outcome of seizures in children with CP was poor needing prolonged course of anticonvulsant medications, polytherapy and higher incidence of refractory seizures and admissions for status epilepticus compared to the control group.

CONCLUSIONS: Cerebral palsy is associated with a higher incidence of seizure disorders, which, in a majority, has its onset in the neonatal period; brain imaging showed abnormal pathology in most affected children, which possibly accounts for the tendency to more refractory seizures in these children.

Epilepsia 2003 Apr;44(4):518-28
Long-term Effects of Status Epilepticus in the Immature Brain Are Specific for Age and Model.
Cilio MR, Sogawa Y, Cha BH, Liu X, Huang LT, Holmes GL.
Department of Neurology, Harvard Medical School, Center for Research in Pediatric Epilepsy, Children's Hospital Boston, Boston, Massachusetts, U.S.A.; and Division of Neurology, Bambino Gesu Children's Hospital, Rome, Italy.
PURPOSE: Status epilepticus (SE) is more common in children than adults and has a high mortality and morbidity rate. SE in adult rats results in long-term disturbances in learning and memory, as well as an enhanced seizure susceptibility to further seizures. In contrast, a number of studies suggest that the immature brain is less vulnerable to the morphologic and physiologic alterations after SE. The goal of this study was to determine whether the long-term consequences of SE during development on hippocampal plasticity and cognitive function are age and model specific. METHODS: We used lithium-pilocarpine (Li-PC) to induce SE at different age points during development (P12, P16, P20) and evaluated the effects of this abnormal neural activity on spatial memory performance and seizure susceptibility in the animals beginning at P55, corresponding to young adulthood. RESULTS: We demonstrated that SE at P12 did not result in any structural or functional changes detectable in adulthood, whereas SE at both P16 and P20 induced cell loss and mossy fiber sprouting within the hippocampus and cognitive impairment when the animals were tested as adults. CONCLUSIONS: Whereas the seizure threshold to generalized seizures was not altered, animals with SE at P20 showed an increased susceptibility to kindling in adulthood.

Exp Neurol 2003 Mar;180(1):88-92
The effect of kindled seizures on the locomotory behavior of Long-Evans rats.
Murphy P, Burnham WM.
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The incidence of attention deficit hyperactivity disorder (ADHD) is higher in children with epilepsy than in the general childhood population. The origin of the symptoms of ADHD seen in children with epilepsy is unknown. This experiment used an animal model to investigate whether seizures could be a cause of the hyperactivity sometimes associated with epilepsy. Sixteen male Long-Evans rats were implanted with electrodes, and 8 of them were kindled until generalized stage 5 seizures were elicited. Eight subjects were handled, but not kindled. The behavior of the rats in the two groups was compared in an open field test. The time spent in four behaviors was measured: exploratory behavior, immobility, eating, and grooming. Rats were tested after 5 stage 5 seizures, after 10 stage 5 seizures, after 15 stage 5 seizures, after a 2-week rest period, and after 5 more stage 5 seizures. Data were analyzed using the Mann-Whitney rank sum test. Twenty-four hours after a seizure, the kindled rats displayed a greater level of exploratory behavior than did the controls. They were not found to differ on any other measure. After a 2-week rest period, the group difference in behavior disappeared. When kindling was reinitiated, the kindled rats again showed increased exploratory behavior. The findings suggest that the increased exploratory behavior found in the kindled rats resulted from recent seizure activity. It may be that the hyperactivity seen in some children with epilepsy also results from recent seizure activity.

Epilepsy Behav 2003 Apr;4(2):124-32
A systematic review of the behavioral effects of levetiracetam in adults with epilepsy, cognitive disorders, or an anxiety disorder during clinical trials.
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This report reviews behavioral adverse events occurring among adults receiving levetiracetam (LEV) or placebo who participated in short-term, placebo-controlled studies in epilepsy (1023), cognitive disorders (719), or anxiety disorders (1510) and epilepsy patients (1393) observed in long-term trials. Behavioral events (affective, psychotic, and suicidal symptoms) were significantly more common among epilepsy patients than cognition or anxiety patients treated with LEV for similar durations (P=0.022). Affective symptoms occurring at 1% or more often in epilepsy placebo-controlled trials included depression (3.8% LEV-2.1% placebo), nervousness (3.8%-1.8%), hostility (2.3%-0.9%), anxiety (1.8%-1.1%), and emotional lability (1.7%-0.2%). Patients with cognitive and anxiety disorders had lower incidences of these symptoms. The incidence of behavioral events in LEV-treated epilepsy patients was lower than rates reported for some other antiepileptic drugs. These data support the hypothesis that some feature related to epilepsy is the cause of many behavioral events rather than the addition of a specific antiepileptic drug.
Very slow EEG responses lateralize temporal lobe seizures
An evaluation of non-invasive DC-EEG

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Background: This study tested the idea that very slow EEG responses (direct current [DC]
potential shifts) could be detected noninvasively during temporal lobe (TL) seizures, and that
these shifts give lateralizing information consistent with that obtained by other methods.

Methods: Seven patients with TL epilepsy (TLE) were recorded with scalp DC-EEG technique at
bedside. All recordings were performed simultaneously with conventional EEG (scalp in five,
and intracranially in two; two patients with scalp recordings were recorded intracranially later).

Seizures in five patients originated in the mesial TL. Ictal DC shifts were evaluated by
comparing them to the temporal evolution of ictal discharges, and by comparing the laterality of
these shifts to the side of seizure onset defined by routine EEG and other presurgical diagnostic
tests.

Results: All seizures (35/35) were associated with negative DC shifts at temporal derivations (30
to 150 µV relative to vertex), beginning at the electrical seizure onset, and lasting for the whole
seizure. In eight seizures (five patients) with documented mesial TL onset, the polarity of the DC
shift was initially positive followed by a negative one after lateral spread of seizure activity. In
all cases, the side of the EEG shift agreed with other diagnostic tests, and, at times, was more
clearly lateralized than the conventional scalp EEG.

Conclusions: DC-EEG recordings are practical and achievable at the bedside. Ictal DC
shifts are consistently observed in scalp recordings in TL seizures, and reliably lateralize
them. This method may hold promise in reducing the need for invasive monitoring in
patients with TLE where other noninvasive tests are equivocal.

Expressive aprosody and amusia as a manifestation of right hemisphere seizures. 
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PURPOSE: Aprosody and amusia are disorders commonly associated with right hemisphere
abnormalities. They are regarded as negative phenomena and usually seen after strokes. We
report a case of a patient who had both expressive aprosody and amusia as a clinical
manifestation of right temporoccipital seizures. METHODS: A 43-year-old woman had a 1-
month history of monotonic speech and difficulty singing. Her examination revealed both
expressive aprosody and amusia. Magnetic resonance imaging of the head was normal, but her EEG revealed several electrographic seizures of right temporooccipital origin. RESULTS: Treatment with phenytoin (PHT) almost immediately caused her speech and singing to return to baseline. A repeated EEG was normal CONCLUSIONS: Seizures of right temporooccipital origin can manifest with expressive aprosody and amusia.

Neurology 2003;60:186-190
How long does it take for partial epilepsy to become intractable?
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Background: Much remains unknown about the natural history of intractable localization-related epilepsy, including how long it typically takes before intractability becomes evident. This information could guide the design of future studies, resolve certain discrepancies in the literature, and provide more accurate information about long-term prognosis.
Methods: Individuals evaluated for resective surgery for refractory localization-related epilepsy were prospectively identified at the time of initial surgical evaluation at seven surgical centers (between 1996 and 2001). The latency time between onset of epilepsy and failure of second medication and history of remission (1 year seizure-free) before surgical evaluation were examined with respect to age at onset, hippocampal atrophy, febrile seizures, and surgical site.
Results: In the 333 patients included in the analysis, latency time was 9.1 years (range 0 to 48) and 26% reported a prior remission before surgery. A prior remission of 5 years was reported by 8.5% of study participants. Younger age at onset was strongly associated with longer latency time (p < 0.0001) and higher probability of past remission (p < 0.0001). In multivariable analyses, age at onset remained as the most important explanatory variable of both latency time and prior remission.
Conclusions: A substantial proportion of localization-related epilepsy may not become clearly intractable for many years after onset. This is especially true of epilepsy of childhood and early adolescent onset. If prospective studies confirm these findings and the underlying mechanisms behind these associations become understood, this raises the possibility of considering interventions that might interrupt such a process and some day prevent some forms of epilepsy from becoming intractable.

CNS Drugs 2003;17(2):101-15
Stimulation of the nervous system for the management of seizures: current and future developments.
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Vagal nerve stimulation (VNS) for the treatment of refractory epilepsy appears to have started from the theory that since VNS can alter the EEG, it may influence epilepsy. It proved effective in several models of epilepsy and was then tried in short-term, open-label and double-blind trials, leading to approval in Canada, Europe and the US. Follow-up observations in these patients demonstrated continued improvement in seizure control for up to 2 years. Close to 50% of treated patients have achieved at least a 50% reduction in seizure frequency. This therapy was also useful as rescue therapy for ongoing seizures in some patients; many patients are more alert. The initial trials were completed in patients >/=12 years of age with refractory partial seizures. Subsequently, similar benefits were shown in patients with tuberous sclerosis complex, Lennox-Gastaut syndrome, hypothalamic hamartomas and primary generalised seizures. Implanting the generator and leads is technically easy, and complications are few. The method of action is largely unknown, although VNS appears to alter metabolic activity in specific brain nuclei. Considering that improvement in mood is frequently found in patients using VNS, it has undergone trials in patients with depression. Other illnesses deserving exploration with this unusual therapy are Alzheimer's disease and autism. Some aspects of VNS have proven disappointing. Although patients have fewer seizures, the number of antiepileptic drugs they take is not significantly reduced. In addition, there is no way to accurately predict the end of life of the generator. Optimal stimulation parameters, if they exist, are unknown. Deep brain stimulation is a new method for controlling medically refractory seizures. It is based on the observation that thalamic stimulation can influence the EEG over a wide area. Several thalamic nuclei have been the object of stimulation in different groups of patients. Intraoperative brain imaging is essential for electrode placement. The procedure is done under local anaesthesia. Experience with this therapy is currently limited, but growing.

*Neurology* 2003;60:564-570

**Meta-analysis of EEG test performance shows wide variation among studies**

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**Background:** EEG results are used for counseling patients with seizures about prognosis and deciding on medications. Published sensitivities of interictal EEG vary widely.

**Objective:** To account for variation in test characteristics between studies.

**Methods:** Meta-analysis. Medline search, 1970 to 2000, of English language studies. Standard methods for meta-analysis of diagnostic test performance were used to determine the ability of EEG results to distinguish between patients who will and will not have seizures. Using linear regression, the authors assessed the influence of readers’ thresholds for classifying the EEG as positive, sample probability of seizure, percent of subjects with prior neurologic impairment, percent treated, and years followed.
**Results:** Twenty-five studies involving 4,912 EEG met inclusion criteria. Specificity (range 0.13 to 0.99) and sensitivity (range 0.20 to 0.91) of epileptiform EEG interpretations varied widely and were heterogeneous by \( \chi^2 \) analysis \( (p < 0.001 \) for each). Diagnostic accuracy of EEG and the thresholds for classifying EEG as positive varied widely. In the multivariate model, differences in readers’ thresholds accounted for 37% of the variance in EEG diagnostic accuracy, and no other reported factors were significant.

**Conclusion:** This analysis suggests that there is wide interreader variation in sensitivity and specificity of EEG interpretations, and that this variation influences the ability of EEG to discriminate between those who will and will not have seizure recurrences. In clinical practice, interpreting the degree to which a positive EEG result predicts increased seizure risk in an individual patient is difficult. Interpreting EEG with higher specificity yields more accurate predictions.

AJNR Am J Neuroradiol 2003 Feb;24(2):218-224

**Magnetization Transfer MR Imaging in Patients with Posttraumatic Epilepsy.**
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**BACKGROUND AND PURPOSE:** Intractable epilepsy is a well-recognized complication following head trauma, and many factors have been implicated in its pathogenesis. This study was performed to determine the severity of tissue damage after severe head injury as assessed with magnetization transfer (MT) MR imaging and the relationship of this damage with seizure intractability. **METHODS:** Forty-four patients, 13 without seizures (disease controls) and 31 with seizures, underwent T1-weighted MT MR imaging 1-10 years after head trauma. Phase-corrected gradient-echo (GRE) imaging was also performed in all patients to look for the presence of hemosiderin. All patients were evaluated for the presence of an MT abnormality beyond an abnormality seen on T2-weighted images, an MT abnormality within a T2 abnormality, and hemosiderin deposition. **RESULTS:** Patients with an MT abnormality beyond a T2 abnormality had a significantly higher intractability of seizures compared with those with an MT abnormality within a T2 abnormality \( (P < .05) \). In addition, the mere presence of hemosiderin deposit was not associated with seizure intractability; however, gliosis around the hemosiderin as seen on T1-weighted MT images was associated with seizure intractability. **CONCLUSIONS:** T1-weighted MT imaging may be of value in predicting the intractability of the seizure in delayed posttraumatic epilepsy.

Neurology 2003;60:405-409

**Hippocampal atrophy and T2-weighted signal changes in familial mesial temporal lobe epilepsy**
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Objective: To correlate the clinical phenotype with hippocampal volumes (HcVs) and signal changes in patients with familial mesial temporal lobe epilepsy (FMTLE).

Methods: FMTLE was defined when at least two first-degree relatives in a family had a clinical-EEG diagnosis of MTLE. Hippocampal formation measurements were performed using 1- to 3-mm coronal T1-weighted MRIs. The presence of hyperintense T2 signal was evaluated by visual analysis. For statistical analyses, analysis of variance, 2 test, and regression analysis were used.

Results: A total of 142 patients from 45 unrelated families were studied: 113 individuals with MTLE (80 with good seizure control) and 29 family members with other seizure types. There were 99 patients (69.7%) with hippocampal atrophy (HA). Sixty-seven of the 99 patients with HA also had a hyperintense T2 signal. Hyperintense T2 signal was associated with more severe HA (p = 0.04). Patients with refractory FMTLE had more frequent HA (p = 0.03) and hyperintense T2 signal (p = 0.004) and more severe atrophy (p < 0.0001). Duration of epilepsy correlated with HcV asymmetry index (r^2 = 0.12, p = 0.0008) and with the more atrophic hippocampi but not with contralateral hippocampi.

Conclusion: In familial mesial temporal lobe epilepsy, seizure severity is variable in affected individuals. Hippocampal atrophy was present in 70% of these patients and 69% of these had an associated hyperintense T2 signal. Although hippocampal atrophy associated with abnormal T2 signal was more frequent and more severe in patients with poor seizure control, it was also frequent in affected individuals across families. These observations suggest that one or more genes resulting in familial mesial temporal lobe epilepsy predisposes both to the clinical features of mesial temporal lobe epilepsy and to the development of hippocampal sclerosis.

An Evaluation of the Effects of Methylphenidate on Outcomes in Adult Epilepsy Patients.

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Purpose. To determine if methylphenidate (MPH) therapy can improve cognition in adult epilepsy patients on multiple antiepileptic drugs (AEDs), we assessed the impact of MPH on seizure activity, quality of life, cognition, and fatigue in patients with a primary diagnosis of localization-related epilepsy.

Methods. This was an open-label, nonrandomized 3-month study. MPH (Ritalin) was added to patients' current antiepileptic drug regimens. Outcome measures included seizure activity, select AED serum concentrations, quality of life (via Quality of Life in
Epilepsy-89 questions (QOLIE-89)), cognition (via Microcog), and fatigue (via a visual analog scale) at baseline and at monthly intervals for the treatment phase.

Results. Eleven patients were enrolled and eight completed this pilot study. Of the eight completing the study, five were seizure-free at baseline and throughout the study. One patient had an increase, one a decrease, and one no change in seizure activity. No serious adverse events were observed. On average, serum AED concentrations changed <10% from baseline to the end of the study. Mean overall QOLIE-89 scores and select domains improved significantly from baseline. All Microcog domains improved from baseline. Fatigue also improved significantly.

Conclusions. Adult epilepsy patients received relief from sedation with MPH and showed an improved quality of life, without significant alteration of seizure control.

W. Curt LaFrance Jr.,* and Orrin Devinsky

Treatment of nonepileptic seizures

Studies on nonepileptic seizures (NES) provide dichotomous data sets: extensive observational findings, but a paucity of controlled treatment data. Psychosocial stressors, whose full impact may lie outside a patient’s awareness, often underlie NES. These stressors, along with patient’s learned patterns of coping, may bring forth or potentiate comorbid psychiatric disorders. Patients with NES often have dysfunction in emotion regulation and family dynamics, as well as unemployment/disability. High percentages of comorbid disorders such as major depressive disorder, post-traumatic stress disorder, and cluster B personality with impulsivity (all disorders associated with serotonin system function) also exist in the NES population. The preliminary observational evidence suggests that specific psychotherapies and pharmacotherapy directed at comorbid conditions may be the most effective treatment for NES.

Epilepsia 2003 Mar;44(3):453-456

The Diagnostic Significance of Video-EEG Monitoring Findings on Pseudoseizure Patients Differs Between Neurologists and Psychiatrists.

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PURPOSE: The diagnosis of psychogenic pseudoseizures has improved with the availability of video-electroencephalography (EEG) monitoring; however, the outcome of this difficult disorder has remained poor. In an attempt to elucidate factors contributing to this poor outcome, we hypothesized that neurologists and psychiatrists differ in their views of the diagnosis and management of psychogenic pseudoseizure patients. METHODS: The hypothesis was tested by using a brief anonymous questionnaire administered to neurologists and psychiatrists at continuing medical education (CME) conferences. RESULTS: We found that neurologists and
psychiatrists differ significantly in their opinion as to the accuracy of the video-EEG procedure; psychiatrists view video-EEG as often inaccurate in the diagnosis of psychogenic pseudoseizures compared with neurologists (p < 0.001). Neurologists, more frequently than psychiatrists, thought that patients' own psychopathology rather than "doctors dropping the ball" was a predominant factor in contributing to therapeutic failure, but this difference between specialties did not reach statistical significance. CONCLUSIONS: Resolving the differences between neurologists and psychiatrists would be helpful in caring for psychogenic pseudoseizure patients. These results support the need to encourage psychiatrists to have an integral involvement in epilepsy centers and to improve the understanding of psychogenic pseudoseizures in both disciplines.

**Overinterpretation of EEGs and Misdiagnosis of Epilepsy.**
Benbadis SR, Tatum WO.
The overinterpretation of EEGs is a known problem that has not been reported specifically. The authors report a series of EEGs on patients who were diagnosed eventually with psychogenic nonepileptic seizures and who had an EEG read as epileptiform. Of the 15 actual records available for review, the overread patterns were wicket spikes (n = 1), hypnagogic hypersynchrony (n = 1), and hyperventilation-induced slowing (n = 1). In the other 12 records, the overread patterns were simple fluctuations of sharply contoured background rhythms or fragmented alpha activity. Rather than well-described normal variants, the overinterpreted patterns tend to be normal fluctuations of background activity.

Clin Neurophysiol 2003 Mar;114(3):569-80
**Quality of EEG in simultaneous EEG-fMRI for epilepsy.**
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It is now possible to record the EEG continuously during fMRI studies. This is a very promising methodology that combines knowledge about neuronal activity and its metabolic response. The EEG recorded inside the fMRI scanner is, however, heavily contaminated by artifacts caused by the high intensity magnetic field and rapidly changing field gradients. Methods have been reported in the literature to reduce or eliminate these artifacts, in particular the ballistocardiogram and the artifact caused by currents induced by rapidly changing magnetic gradients. Nevertheless, recording the EEG simultaneously with fMRI remains an extremely delicate operation. In addition the use of artifact removal methods has only been reported by the laboratories in which they were developed. We report here the practical procedures we developed to reduce artifacts in a series of 10 epileptic patients, in the context of the visualization of epileptic spikes. We illustrate the effectiveness of methods designed to remove the scanning artifact and present new methods for removing the ballistocardiographic artifact. We present and evaluate techniques to obtain an EEG of good quality when performing simultaneous EEG and fMRI studies.
J Atten Disord 2002;6 Suppl 1:S7-16

**Current concepts on the neurobiology of Attention-Deficit/Hyperactivity Disorder.**
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Attention-Deficit/Hyperactivity Disorder (ADHD) is an early onset, clinically heterogeneous disorder of inattention, hyperactivity, and impulsivity. In contrast to the widespread acceptance of ADHD as a childhood diagnosis, its prevalence in adults and its implications for clinical practice remain a source of controversy. Throughout the lifecycle, a key clinical feature observed in ADHD patients is comorbidity with Conduct Depressive, Bipolar, and Anxiety disorders. Family studies consistently support the assertion that ADHD runs in families. Heritability data from twin studies of ADHD attribute about 80 percent of the etiology of ADHD to genetic factors. Adoption studies of ADHD also implicate genes in its etiology. Molecular genetic data are bolstered by considerations suggesting that DRD4 and DAT genes may be relevant for ADHD. Independently of genes, prenatal exposure to nicotine and psychosocial adversity have also been identified as risk factors for ADHD. Structural and functional imaging studies consistently implicate catecholamine-rich fronto-subcortical systems in the pathophysiology of ADHD. The effectiveness of stimulants, along with animal models of hyperactivity, point to catecholamine disruption as at least one source of ADHD brain dysfunction. Although not entirely sufficient, changes in dopaminergic and noradrenergic function appear necessary for the clinical efficacy of pharmacological treatments for ADHD, providing support for the hypothesis that alteration of monoaminergic transmission in critical brain regions may be the basis for therapeutic action in ADHD.

Psychoneuroendocrinology 2003 Apr;28(3):376-85

**The combined dexamethasone-CRH test before and after repetitive transcranial magnetic stimulation (rTMS) in major depression.**
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BACKGROUND: Hypothalamic-pituitary-adrenocortical (HPA) dysregulation assessed by the combined dexamethasone corticotropin releasing hormone test (DEX/CRH test) has been demonstrated to normalize after successful antidepressant pharmacotherapy. Here, we investigated whether repetitive transcranial magnetic stimulation (rTMS) also leads to a normalization of HPA system activity in depressed patients. METHODS: Thirty-seven medication free patients suffering from a major depressive episode (DSM-IV) underwent a DEX/CRH test before and after 13 daily sessions of left prefrontal rTMS in an open trial. RESULTS: There was an overshoot of CRH-induced cortisol release that was not affected by rTMS treatment. Postdexamethasone cortisol levels prior to CRH challenge decreased in responders after rTMS treatment, whereas no change of CRH-induced adrenocorticotropic hormone (ACTH) and cortisol release in responders or nonresponders was observed. CONCLUSIONS: The persisting HPA system hyperactivity after rTMS suggests a high risk for relapse and therefore argues for an immediate maintenance therapy in patients responding to this treatment.

Neuroendocrine Abnormalities in Fibromyalgia
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Fibromyalgia is a disorder of unknown etiology characterized by chronic, widespread musculoskeletal pain and symptoms such as fatigue, poor sleep, gastrointestinal complaints, and psychologic problems that are similar to those experienced by patients with hormone deficiencies. This review summarizes the available data on the neuro-endocrine function in fibromyalgia, including data on hormone secretion, circadian phase, and autonomic nervous system function. Studies suggest that there may be lower activity of a number of hypothalamic-pituitary-peripheral gland axes and altered autonomic nervous system function in patients with fibromyalgia. These reductions in activity are mild to moderate and do not result from alterations in circadian rhythms. The reduced hormonal and autonomic responses appear to reflect an impairment in the hypothalamic or central nervous system response to stimuli rather than a primary defect at the level of the pituitary gland or the peripheral glands. A combination of multiple, mild impaired responses may lead to more profound physiologic and clinical consequences as compared with a defect in only one system, and could contribute to the symptoms of fibromyalgia.


Mild cognitive impairment: Conceptual issues and structural and functional brain correlates.
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Mild cognitive impairment (MCI) is a prevalent condition among older adults that carries a high risk of progression to Alzheimer's disease or other dementias. Given the potential for
delaying or preventing the onset of dementia, efforts aimed at early detection and early intervention are important. The current paper reviews the conceptualization and diagnosis of MCI, assessment of memory complaints and deficits in the elderly, as well as recent research on the neurobiological basis of the disorder, including neurochemical, structural, and functional neuroimaging findings.

Cereb Cortex 2003 Mar;13(3):265-73
FMRI evidence for an organization of prefrontal cortex by both type of process and type of information.
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Neuroimaging evidence is conflicting regarding whether human prefrontal cortex (PFC) shows functional organization by type of processes engaged or type of information processed. Most studies use complex working or long-term memory tasks requiring multiple processes and the combinations of processes recruited for different materials may vary. Using functional magnetic resonance imaging (fMRI) and simple tasks suggested by a component process approach, we found activity in left PFC when participants thought about (refreshed) a just-seen item and in right PFC when participants noted whether an item had been presented previously. Furthermore, the distribution of activation in left or right PFC varied with type of information. Thus, at the component process level, PFC shows functional organization by both process and type of information.

Appl Psychophysiol Biofeedback 2002 Dec;27(4):261-70
EEG signature and phenomenology of alpha/theta neurofeedback training versus mock feedback.
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Alpha/theta (a/t) neurofeedback training has in the past successfully been used as a complementary therapeutic relaxation technique in the treatment of alcoholism. In spite of positive clinical outcomes, doubts have been cast on the protocol's specificity when compared to alternative relaxation regimes. This study investigated the basic tenet underlying the a/t training rationale, that accurate a/t feedback representation facilitates the generation of these frequency components. Two groups of healthy volunteers were randomly assigned to either (a) real contingent a/t feedback training or (b) a noncontingent mock feedback control condition. The groups were compared on measures of theta/alpha (t/a) ratios within and across training sessions, as well as activational self-report scales after each session. The contingent a/t feedback group displayed significant within-session t/a ratio increments not evident in the mock control group, as well as higher overall t/a ratios in some but not all of the training sessions. No differences were found between the groups in terms of subjective activational phenomenology, in that both groups
reported significantly lower levels of activation after training sessions. The data demonstrate that irrespective of considerations of clinical relevance, accurate a/t neurofeedback effectively facilitates production of higher within-session t/a ratios than do noncontingent feedback relaxation.

Clin Neurophysiol 2003 Feb;114(2):319-28

**EEG activity in girls with attention-deficit/hyperactivity disorder.**

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**OBJECTIVE:** This study investigated the EEG of girls with Attention-deficit/hyperactivity disorder (ADHD).

**METHODS:** Subjects consisted of 100 girls with ADHD between the ages of 8 and 12 years and 40 age- and gender-matched controls. EEG was recorded from 21 sites during an eyes-closed resting condition and Fourier transformed to provide estimates for total power, and relative power in the delta, theta, alpha and beta bands. Factor analysis was used to group sites into 3 regions, covering frontal, central and posterior regions. The total ADHD group was compared to the control group as well as the data being subjected to cluster analysis.

**RESULTS:** The ADHD subjects had greater total power, more relative theta, and less relative delta, alpha and beta than controls. Cluster analysis indicated the presence of two distinct EEG clusters of girls with ADHD. These were (a) a large subgroup characterized by increased total power, more relative theta, and less relative delta and beta than control subjects; and (b) a small subgroup with a substantially-increased amount of high amplitude theta activity, with deficiencies in all other bands.

**CONCLUSIONS:** These results indicate that girls with ADHD exhibit abnormalities in their EEGs, but there is far less variance in their EEG profiles than is found in boys with the disorder. The results also suggest that there may be distinct groups of girls with ADHD who are not being referred for clinical treatment. Recommendations are made for further research in this population. This study is significant in that it is the first major study to separately investigate the EEG of girls with ADHD.


**Novel treatments for attention-deficit/hyperactivity disorder in children.**

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Optimal medications for children with attention-deficit/hyperactivity disorder (ADHD) would be effective, well tolerated, and long acting and not cause mood swings or worsen comorbid conditions. Current medications work on brain dopamine and/or norepinephrine systems, which are thought to be involved in ADHD. The medication class with the most evidence of efficacy in ADHD is stimulants, but they may be abused, are effective for only 4 to 12 hours, and may cause mood swings or increase tic severity. In recent years, alternative treatments have been explored. Tri cyclic antidepressants have efficacy comparable to that of stimulants but may cause constipation, dry mouth, tremors, blood pressure changes, and
potentially serious side effects including cardiac conduction and repolarization delays. Monoamine oxidase inhibitors may improve ADHD symptoms but are associated with severe dietary restrictions. Serotonin reuptake inhibitors have little or no effect in ADHD but may improve comorbid depression. Bupropion, although less effective than stimulants, may improve both ADHD symptoms and comorbid depression. Antihypertensive agents may improve impulsivity, hyperactivity, and comorbid tics but cause sedation or rebound hypertension. Atomoxetine, which is being developed for ADHD, reduces symptoms of ADHD without exacerbating comorbid conditions and is associated with only minor side effects, including subtle changes in blood pressure and heart rate. Before prescribing a treatment, physicians should consider the appropriateness and effectiveness of any medication for children with ADHD, who may be less tolerant of side effects and less able to monitor and express concerns about their well-being than adults.

Neuropsychologia 2003;41(5):634-43

**Temporary and permanent signs of interhemispheric disconnection after traumatic brain injury.**

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The corpus callosum is frequently damaged by closed head traumas, and the resulting deficits of interhemispheric communication may vary according to the specific position of the lesion within the corpus callosum. This paper describes a single case who suffered a severe traumatic brain injury resulting in a lesion of the posterior body of the corpus callosum. Among the classical symptoms of interhemispheric disconnection, left hand anomia, left upper limb ideomotor dyspraxia, left visual field dyslexia and dysnomia, and left ear suppression in a dichotic listening task were observed shortly after the injury but recovered completely or almost completely with the passage of time. The only symptom of interhemispheric disconnection which was found to persist more than 4 years after the injury was an abnormal prolongation of the crossed-uncrossed difference in a simple visuomotor reaction time task. This prolongation was comparable with that observed in subjects with complete callosal lesions or agenesis. The results suggest that the posterior body of the corpus callosum may be an obligatory interhemispheric communication channel for mediating fast visuo-motor responses. The transient nature of other symptoms of interhemispheric disconnection suggests a relatively wide dispersion of fibers with different functions through the callosal body, such that parts of them can survive a restricted lesion and allow functional recovery of hemispheric interactions. An assessment of the evolution in time of symptoms of interhemispheric disconnection following restricted callosal lesions may reveal fine and coarse features of the anatomo-functional topography of the corpus callosum.

J Clin Psychiatry 2002;63 Suppl 14:22-6

**Anxiety associated with comorbid depression.**
Moller HJ.
Historically, the clinical term for mixed depression and anxiety was anxious depression. With the publication of DSM-III-R, 2 categories were established for the purpose of classifying disorders that involve both anxiety and depression, and that classification system is currently used in DSM-IV as well. These more specific diagnostic criteria have given us a much better understanding of the anxiety spectrum, but have created a need for a better understanding of the place of benzodiazepines in clearly defined indications on the anxiety spectrum. In spite of warnings about side effects, misuse, and dependence, benzodiazepines are frequently prescribed as adjunctive therapy to antidepressants for comorbid anxiety and depression. This article presents data on the prevalence, course, and outcome of comorbid anxiety and depression. It also compares efficacy data from trials of benzodiazepines used alone and in combination with antidepressants for the treatment of anxiety disorders comorbid with depression.

**Effects of depressed mood on objective and subjective measures of attention.**
Farrin L, Hull L, Unwin C, Wykes T, David A.
Received May 21, 2001.

People with depression report frequent cognitive failures, but objective measures of cognition show mixed results. Some studies show impairment on effortful tasks. The relationship between subjective and objective cognitive failures was studied in 102 "depressed" or "nondepressed" UK servicemen, grouped by Beck Depression Inventory scores with a cutoff score of 10. Participants were administered cognitive tests including the Sustained Attention to Response Task (SART), a laboratory measure of vigilance that has revealed increased attentional lapses in traumatic brain injury patients. The depressed men made more errors on SART than the nondepressed men (P=0.012) but reported much higher incidences of cognitive failures on a standardized questionnaire (P=0.0001). The depressed men's SART reaction times slowed following an error, a pattern different from that of brain-injured subjects. Nonclinical depressed subjects may respond "catastrophically" to errors, heightening the subjective sense of failure and contributing to the strong relationship between subjectively reported cognitive failures and depression.

**A review of electrophysiology in attention-deficit/hyperactivity disorder: I. Qualitative and quantitative electroencephalography.**
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OBJECTIVE: This article reviews the electroencephalography (EEG) literature in relation to attention-deficit/hyperactivity disorder (AD/HD).METHODS: The review briefly outlines the history of the disorder, focusing on the changing diagnostic systems which both reflect and
constrain research into AD/HD. Both qualitative and quantitative EEG studies are examined, and their results are discussed in relation to various models of AD/HD. Implications of these data for future research and development in AD/HD are considered.

**RESULTS:** In terms of resting EEG, elevated relative theta power, and reduced relative alpha and beta, together with elevated theta/alpha and theta/beta ratios, are most reliably associated with AD/HD. Theta/alpha and theta/beta ratios also discriminate diagnostic subgroups of AD/HD. Recent studies of EEG heterogeneity in this disorder indicate the existence of different profiles of cortical anomalies which may cut across diagnostic types.

**CONCLUSIONS:** The research to date has identified a substantial number of EEG correlates of AD/HD which hold promise for improving our understanding of the brain dysfunction(s) underlying the disorder. Further work in this field may benefit from a broader conceptual approach, integrating EEG and other measures of brain function.

Appl Psychophysiol Biofeedback 2002 Dec;27(4):231-49
The effects of stimulant therapy, EEG biofeedback, and parenting style on the primary symptoms of attention-deficit/hyperactivity disorder.
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One hundred children, ages 6-19, who were diagnosed with attention-deficit/hyperactivity disorder (ADHD), either inattentive or combined types, participated in a study examining the effects of Ritalin, EEG biofeedback, and parenting style on the primary symptoms of ADHD. All of the patients participated in a 1-year, multimodal, outpatient program that included Ritalin, parent counseling, and academic support at school (either a 504 Plan or an IEP). Fifty-one of the participants also received EEG biofeedback therapy. Posttreatment assessments were conducted both with and without stimulant therapy. Significant improvement was noted on the Test of Variables of Attention (TOVA; L. M. Greenberg, 1996) and the Attention Deficit Disorders Evaluation Scale (ADDES; S. B. McCarney, 1995) when participants were tested while using Ritalin. However, only those who had received EEG biofeedback sustained these gains when tested without Ritalin. The results of a Quantitative Electroencephalographic Scanning Process (QEEG-Scan; V. J. Monastra et al., 1999) revealed significant reduction in cortical slowing only in patients who had received EEG biofeedback. Behavioral measures indicated that parenting style exerted a significant moderating effect on the expression of behavioral symptoms at home but not at school.

Neurobiol Learn Mem 2002 Nov;78(3):625-36
Limbic-striatal memory systems and drug addiction.
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Drug addiction can be understood as a pathological subversion of normal brain learning and memory processes strengthened by the motivational impact of drug-associated stimuli, leading to
the establishment of compulsive drug-seeking habits. Such habits evolve through a cascade of complex associative processes with Pavlovian and instrumental components that may depend on the integration and coordination of output from several somewhat independent neural systems of learning and memory, each contributing to behavioral performance. Data are reviewed that help to define the influences of conditioned Pavlovian stimuli on goal-directed behavior via sign-tracking, motivational arousal, and conditioned reinforcement. Such influences are mediated via defined corticolimbic-striatal systems converging on the ventral striatum and driving habit-based learning that may depend on the dorsal striatum. These systems include separate and overlapping influences from the amygdala, hippocampus, and cingulate and medial prefrontal cortex on drug-seeking as well as drug-taking behavior, including the propensity to relapse.

A recent symposium on cranial fascial pain is discussed on the web on information on chronic pain. Http://www.ninds.nih.gov/healthandmedical/pubs/pain.htm

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NCBI Genes and Disease Webpage
Www.ncbi.nlm.nih.gov/disease/Alzheimer.html
Subjective rating scales: science or art?
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Subjective rating scales are widely used in almost every aspect of ergonomics research and practice for the assessment of workload, fatigue, usability, annoyance and comfort, and lesser known qualities such as urgency and presence, but are they truly scientific? This paper raises some of the key issues as a basis for debate. First, it is argued that all empirical observations, including those conventionally labelled as 'objective', are unavoidably subjective. Shared meaning between observers, or intersubjectivity, is the key criterion of scientific probity. The practical steps that can be taken to increase intersubjective agreement are discussed and the well-known sources of error and bias in human judgement reviewed. The role of conscious experience as a mechanism for appraising the environment and guiding behaviour has important implications for the interpretation of subjective reports. The view that psychometric measures do not conform to the requirements of truly 'scientific' measurement is discussed. Human judgement of subjective attributes is essentially ordinal and, unlike physical measures, can be matched to interval scales only with difficulty, but ordinal measures can be used successfully both to develop and test substantive theories using multivariate statistical techniques. Constructs such as fatigue are best understood as latent or inferred variables defined by a set of manifest or directly observed indicator variables. Both construct validity and predictive validity are viewed from this perspective and this helps to clarify several problems including the dissociation between measures of different aspects of a given construct, the question of whether physical (e.g. physiological) measures should be preferred to subjective measures and whether a single measure of constructs which are essentially multidimensional having both subjective and physical components is desirable. Finally, the fitness of subjective ratings to different purposes within the broad field of ergonomics research is discussed. For testing of competing hypotheses concerning the mechanisms underlying human performance, precise quantitative predictions are rarely needed. The same is frequently true of comparative evaluation of competing designs. In setting design standards, however, something approaching the level of measurement required for precise quantitative prediction is required, but this is difficult to achieve in practice. Although it may be possible to establish standards within restricted contexts, general standards for broadly conceived constructs such as workload are impractical owing to the requirement for representative sampling of tasks, work environments and personnel.
Physiological, metabolic, and performance implications of a prolonged hill walk: influence of energy intake.
Ainslie PN, Campbell IT, Frayn KN, Humphreys SM, MacLaren DP, Reilly T.

We aimed to examine the effects of different energy intakes on a range of responses that are relevant to the safety of hill walkers. In a balanced design, 16 men completed a strenuous self-paced mountainous hill walk over 21 km, under either a low-energy (2.6 MJ; 616 kcal) intake (LEI) or high-energy (12.7 MJ; 3,019 kcal) intake (HEI) condition. During the hill walk, rectal temperatures were measured continuously, and blood samples for the analysis of metabolites and hormones were drawn before breakfast and immediately after the walk. Subjects also completed a battery of performance tests that included muscular strength, reaction times, flexibility, balance, and kinesthetic differentiation tests. During the LEI, mean blood glucose concentrations leveled off at the low-middle range of normoglycemia, whereas, on the HEI, they were significantly elevated compared with the LEI. The maintained blood glucose concentrations, during the LEI, were probably mediated via the marked fat mobilization, reflected by a two- to fivefold increase in nonesterified fatty acids, 3-hydroxybutyrate, and glycerol concentrations. The LEI group showed significantly slower one- and two-finger reaction time, had an impaired ability to balance, and were compromised in their ability to maintain body temperature, when compared with the HEI group. The modestly impaired performance (particularly with respect to balance) and thermoregulation during the LEI condition may increase susceptibility to both fatigue and injury during the pursuit of recreational activity outdoors.

Sleep EEG patterns and fatigue of middle-aged and older female family caregivers providing routine nighttime care for elderly persons at home.
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The sleep EEGs and fatigue of 9 female family caregivers (age M=65 yr.) and 9 female noncaregivers (age M=67 yr.) were measured during two successive nights at their houses. Perceived quality of sleep was measured by the Sleep Evaluation Questionnaire. Fatigue was measured by a self-rated questionnaire, the Perceived Symptoms of Fatigue, and by critical flicker fusion (CFF) frequency. The caregivers had a significantly higher percentage of Stage 1 and a lower percentage of Stage 2 during the 2nd cycle and a higher percentage of Stages 3+4 during the 3rd cycle than those of the noncaregivers. Caregivers had significantly higher percentages of EEG waves of 7-9 Hz in the 1st cycle and 6-9 Hz in the 2nd cycle and significantly lower percentages of 2-3 Hz in the 1st cycle than those of the noncaregivers. The caregivers reported a lower quality of sleep and higher perceived fatigue symptoms and also lower CFF frequency (increased physiological fatigue) than noncaregivers. The caregivers' sleep EEGs were associated with their higher sleep needs and fatigue.

Psychosom Med 2002 Nov-Dec;64(6):951-62
Hypothalamic-pituitary-adrenal axis reactivity in chronic fatigue syndrome and health under psychological, physiological, and pharmacological stimulation.
OBJECTIVES: Subtle alterations of the hypothalamic-pituitary-adrenal (HPA) axis in chronic fatigue syndrome (CFS) have been proposed as a shared pathway linking numerous etiological and perpetuating processes with symptoms and observed physiological abnormalities. Because the HPA axis is involved in the adaptive responses to stress and CFS patients experience a worsening of symptoms after physical and psychological stress, we tested HPA axis functioning with three centrally acting stress tests. METHODS: We used two procedures mimicking real-life stressors and compared them with a standardized pharmacological neuroendocrine challenge test. CFS patients were compared with healthy control subjects regarding their cardiovascular and endocrine reactivity in a psychosocial stress test and a standardized exercise test, and their endocrine response in the insulin tolerance test (ITT). RESULTS: Controlling for possible confounding variables, we found significantly lower ACTH response levels in the psychosocial stress test and the exercise test, and significantly lower ACTH responses in the ITT, with no differences in plasma total cortisol responses. Also, salivary-free cortisol responses did not differ between the groups in the psychosocial stress test and the exercise test but were significantly higher for the CFS patients in the ITT. In all tests CFS patients had significantly reduced baseline ACTH levels. CONCLUSIONS: These results suggest that CFS patients are capable of mounting a sufficient cortisol response under different types of stress but that on a central level subtle dysregulations of the HPA axis exist.

Unconscious amygdalar fear conditioning in a subset of chronic fatigue syndrome patients.
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Here, a novel hypothesis for chronic fatigue syndrome (CFS) is proposed. CFS may be a neurophysiological disorder focussing on the amygdala. During a 'traumatic' neurological event often involving acute psychological stress combined with a viral infection or other chemical or physiological stressor, a conditioned network or 'cell assembly' may be created in the amygdala. The unconscious amygdala may become conditioned to be chronically sensitised to negative symptoms arising from the body. Negative signals from the viscera or physiological, chemical and dietary stressors, become conditioned stimuli and the conditioned response is a chronic sympathetic outpouring from the amygdala via various brain pathways including the hypothalamus. This cell assembly then produces the CFS vicious circle, where an unconscious negative reaction to symptoms causes immune reactivation/dysfunction, chronic sympathetic stimulation, leading to sympathetic dysfunction, mental and physical exhaustion, and a host of other distressing symptoms and secondary complications. And these are exactly the symptoms that the amygdala and associated limbic structures are trained to monitor and respond to, perpetuating a vicious circle. Recovery from CFS may involve projections from the medial prefrontal cortex to the amygdala, to control the amygdala's expressions. I shall firstly discuss predisposing, precipitating, and perpetuating factors involved in the possible etiology of chronic
fatigue syndrome (CFS), followed by the patient's experience of the illness. Finally, I shall look at a suggested explanation for the symptoms of CFS.

Anesth Analg 2002 Nov;95(5):1446-50, table of contents

Physiological and psychological influences on postoperative fatigue.
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Fatigue is common after major surgery and delays recovery. We studied the role of physiological and psychological factors in determining fatigue and physical well being after surgery in 102 patients undergoing primary hip arthroplasty. Self-administered questionnaires were used to measure the intensity of feelings of fatigue, vigor, depression, and subjective physical well being on the day before surgery, on the third and seventh postoperative days, and 1 and 6 mo after surgery. The physiological response to surgery was determined by sequential measurements of circulating norepinephrine, epinephrine, cortisol, interleukin-6, and C-reactive protein during the 7 days after surgery. The peak value of each variable was used for statistical analysis. Physical well being decreased significantly at 3 and 7 days but increased significantly at 1 and 6 mo. Fatigue decreased significantly at 1 and 6 mo. Multiple regression analysis showed that the main predictor of worse physical well being at 3 days was the size of the C-reactive protein response. Subsequently, the main predictor was the level of preoperative well being. The severity of fatigue and vigor after surgery were predicted mostly by the preoperative levels of the respective variable. We conclude that fatigue after hip arthroplasty was not predicted by physiological variables but was largely predicted by preoperative levels of fatigue. IMPLICATIONS: Fatigue is common after major surgery and delays recovery. It is usually attributed to the physiological response to surgery. We studied patients undergoing hip arthroplasty and found that the severity of postoperative fatigue was not predicted by physiological changes. Instead, it was predicted by the preoperative level of fatigue.

Aviat Space Environ Med 2002 Jul;73(7):654-64

Controlled breaks as a fatigue countermeasure on the flight deck.
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BACKGROUND: A major challenge for flight crews is the need to maintain vigilance during long, highly automated nighttime flights. No system currently exists to assist in managing alertness, and countermeasure options are limited. Surveys reveal many pilots use breaks as an in-flight countermeasure, but there have been no controlled studies of their effectiveness. HYPOTHESIS: We hypothesized that brief, regular breaks could improve alertness and performance during an overnight flight. METHOD: A 6-h, uneventful, nighttime flight in a Boeing 747-400 flight simulator was flown by fourteen two-man crews. The 14 subjects in the treatment group received 5 short breaks spaced hourly during cruise; the 14 subjects in the control group received 1 break in the middle of cruise. Continuous EEG/EOG, subjective*
sleepiness, and psychomotor vigilance performance data were collected. RESULTS: During the latter part of the night, the treatment group showed significant reductions for 15 min post-break in slow eye movements, theta-band activity, and unintended sleep episodes compared with the control group. The treatment group reported significantly greater subjective alertness for up to 25 min post-break, with strongest effects near the time of the circadian trough. There was no evidence of objective vigilance performance improvement at 15-25 min post-break, with expected performance deterioration occurring due to elevated sleep drive and circadian time. CONCLUSIONS: The physiological and subjective data indicate the breaks reduced nighttime sleepiness for at least 15 min post-break and may have masked sleepiness for up to 25 min, suggesting the potential usefulness of short-duration breaks as an in-flight fatigue countermeasure.

Psychosom Med 2003 Jan-Feb;65(1):129-36

Single-photon emission computerized tomography and neurocognitive function in patients with chronic fatigue syndrome.

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OBJECTIVE: The purposes of this study were to compare functional imaging under control and experimental conditions among patients with chronic fatigue syndrome (CFS) and healthy persons and to examine perceived and objective performance on a test of attention and working memory previously found to be difficult for persons with CFS. METHODS: Single-photon emission computerized tomography scans were completed on 15 subjects with CFS and 15 healthy persons twice: at rest and when performing the Paced Auditory Serial Addition Test (PASAT). RESULTS: No group differences were found for performance on the PASAT despite CFS subjects' perceptions of exerting more mental effort to perform the task than healthy subjects. Inspection of the aggregate scans by group and task suggested a pattern of diffuse regional cerebral blood flow among subjects with CFS in comparison with the more focal pattern of regional cerebral blood flow seen among healthy subjects. Between-group region-of-interest analysis revealed that although CFS subjects showed less perfusion in the anterior cingulate region, the change in CFS subjects' activation of the left anterior cingulate region during the PASAT was greater than that observed for healthy subjects. The differences were not attributable to lesser effort by the subjects with CFS, confounding effects of mood perturbation, or to poorer performance on the experimental task. CONCLUSIONS: Further research regarding CFS subjects' diffuse cerebral perfusion and its relationship to inefficient neuropsychological performance is warranted.

Psychological Medicine (2003), 33:263-281

Fatigue in a community sample of twins

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Background. Fatigue is a complex symptom associated with many physiological, psychological and pathological processes. Its correlates and typology remain inadequately understood.

Method. These data were from two large, longitudinal twin studies. Trained interviewers enquired as to the presence of a ≥5 day period in the previous year of fatigue or tiredness that interfered with daily activities. A range of potential correlates was assessed in a structured interview: demography; health beliefs; the presence of nine physical disorders; mood, anxiety and addictive disorders; neuroticism and extraversion; recollections of parental rearing; and nine stressful life events. Statistical analyses included logistic regression, CART, MARS, latent class analysis and univariate twin modelling.

Results. Data were available for interfering fatigue (IF) on 7740 individual twins (prevalence 9.9% in the previous year). IF was significantly associated with 42 of 52 correlates (most strongly with major depression, generalized anxiety disorder, reported major health problems and neuroticism). Multivariate analyses demonstrated that IF is a highly complex construct with different sets of correlates in its subtypes. There were two broad clusters of correlates of IF: (a) major depression, generalized anxiety disorder and neuroticism; and (b) beliefs of ill health coexisting with alcoholism and stressful life events. Twin analyses were consistent with aetiological heterogeneity – genetic effects may be particularly important in women and shared environmental effects in men.

Conclusions. IF is a complex and common human symptom that is highly heterogeneous. More precise understanding of the determinants of IF may lead to a fuller understanding of more extreme conditions like chronic fatigue syndrome.
The reliance on self-report outcome measures in clinical trials of graded activity-oriented cognitive-behavior therapy in chronic fatigue syndrome (CFS) makes it difficult to draw definitive conclusions about actual behavioral change. The participant in this case study was a 52-year-old married male with CFS who was working full-time. Outcome measures included a step counter to objectively measure physical activity as well as a daily diary measure of exercise activity and in vivo ratings of perceived energy, fatigue, and affect. The following psychometric instruments were also used: the CFS Symptom Inventory, the SF-36, the Beck Depression Inventory, and the Beck Anxiety Inventory. The 26-session graded activity intervention involved gradual increases in physical activity. From baseline to treatment termination, the patient's self-reported increase in walk time from 0 to 155 min a week contrasted with a surprising 10.6% decrease in mean weekly step counts. The final follow-up assessment revealed a "much improved" global rating, substantial increases in patient-recorded walk time and weight lifting intensity, yet a relatively modest increment in weekly step counts. It appeared that improvement was associated with mood-enhancing, stress-reducing activities that were substituted for stress-exacerbating activities.

PSEUDODEMENTIA

J Affect Disord 2002 May;69(1-3):159-66
Brain single photon emission computed tomography findings in depressive pseudodementia patients.
Cho MJ, Lyoo IK, Lee DW, Kwon JS, Lee JS, Lee DS, Jung JK, Lee MC.
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BACKGROUND: Recently, there have been studies suggesting that depressive pseudodementia would include early-stage dementing disorder. Through the comparison of the (99m)Tc-HMPAO single photon emission computed tomography (SPECT) image of depressive pseudodementia subjects, healthy comparison subjects, depressed subjects free of cognitive impairment, and dementia of Alzheimer's type (DAT) subjects, we aimed to see part of pathophysiology of the depressive pseudodementia of elderly patients. METHODS: Study subjects consisted of seven patients with depressive pseudodementia, seven healthy comparison subjects, seven patients with depression free of cognitive impairment, and eleven patients with DAT. Depression patients were diagnosed according to DSM-III-R. DAT patients were diagnosed by DSM III-R and NINCDS-ADRDA criteria of DAT. Other measures for assessment include Hamilton Rating Scale for Depression and Mini Mental State Exam. All underwent (99m)Tc-HMPAO SPECT scan. The images of each group were analyzed using statistical parametric mapping of Friston, which compares the images on voxel-by-voxel basis. RESULTS:
The results were as follows (1) The DAT group showed significant decreases of cerebral blood flow (CBF) in the right frontal, right temporal region, and both parietal regions as compared with control group (P<0.05). (2) The depression group showed a significant decrease of CBF in the left frontal region as compared with control group (P<0.05). (3) The depressive pseudodementia group showed significant decreases of CBF in both parietal regions as compared with control group (P<0.05). (4) The depressive pseudodementia group showed significant decreases of CBF in the right temporal region and both parietal regions as compared with depression group (P<0.05). (5) The DAT group showed significant decreases of CBF in the right temporal region, both frontal regions, and both parietal regions as compared with depressive pseudodementia group (P<0.05). LIMITATIONS: The small number of subjects may make it difficult to generalize from our results. Because decreased CBF in depressive pseudodementia is found while the subjects were depressed, we cannot tell whether it is a state marker or a trait marker. CONCLUSIONS: The depressive pseudodementia group showed decreased CBF in the temporo-parietal region, similar to that of the DAT group and different from that of the depression group.

[Depressive pseudodementia]
[Article in German]
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Elderly depressive patients complaining about cognitive symptoms are at particular risk of being labelled as demented. It is well documented that depressive disorders frequently cause mild cognitive deficits which manifest in psychometric procedures. A wide spectrum of potentially reversible cognitive deficits related to a depressive syndrome are summarized under the term of "Depressive Pseudodementia (DPD)". Most depressive patients who are referred to "DPD" suffer from cognitive dysfunctions outside the range of dementia. The clinical interface between depression and dementia is complex. There is some evidence that depression may be a risk factor for the expression of Alzheimer's disease in later life and that depression may occur as a prodrome for Alzheimer dementia. Moreover, depression often complicates the course of dementing disorders. However, there is no evidence that depressive disorders cause dementia without coexisting depressive symptoms. It is essential to search for depressive symptoms even after cognitive symptoms have been found.

FUNCTIONAL DISORDERS

Spinal Cord 2002 Jul;40(7):327-34
Conversion motor paralysis disorder: overview and rehabilitation model.
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It is important to consider a differential diagnosis between paralysis on an organic basis and paralysis and disability due to psychological mechanisms in people with physical impairment secondary to trauma, without evidence of organic etiology. We review the most dramatic type of conversion disorder (CD)-'Conversion Motor Paralysis'. Recent important medical literature concerning the accepted treatment and rehabilitation management will be reviewed and discussed. The inter-disciplinary in-patient team management approach in a rehabilitation setting offers the benefits of a comprehensive assessment and treatment. The diagnosis is temporary and conditional, since there may be a long delay until the appearance of organic findings. A complete medical assessment is essential in order to rule out any possibility of an organic etiology. In as many as 25% to 50% of patients diagnosed as conversion, an organic medical diagnosis was found.

Child Abuse Negl 2002 May;26(5):537-49
On the importance of motivation in Munchausen by Proxy: the case of Kathy Bush.
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The recent trial and conviction of Kathy Bush for abusing her daughter is used to illustrate (1) the nature of the motivation, in at least some cases of MBP, and (2) the importance of distinguishing the motivation found in MBP from that found in other forms of child abuse and other conditions involving factitious illness production.

Child Abuse Negl 2002 May;26(5):525-36
Beyond collusion: active illness falsification.
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OBJECTIVE: This article explores the relationship between factitious disorder by proxy victimization and the genesis of factitious disorder in young people. It is hoped that this will aid in our understanding of how some illness falsification behaviors may be learned and transmitted within the family system. METHOD: A discussion of the origins of adult factitious disorder and recent findings on the phenomenon of illness falsification in children and adolescents is integrated with some of the more ambiguous or "blended" cases which combine primary falsification by the youngster with caregiver collusion. Those less easily classified cases of factitious illness which fall in the gray areas, containing elements of both independent illness falsification by a child or adolescent with an earlier history of collusion with a parent's Munchausen by Proxy disorder, are proposed as a type of transitional case which may help us better understand the process by which illness falsification is learned. RESULTS: The literature on illness falsification in adults supports the possibility that adult factitious disorder may have its origins in adolescence or perhaps even earlier. Several cases are identified which suggest that some youngsters independently falsifying illness may have had earlier experiences of Munchausen by Proxy victimization or perhaps experienced the modeling or encouragement of illness falsification by a caregiver. Certain elements of the child victim experience, including efforts to overcome feelings of powerlessness, chronic lack of control, and disappointment in the physician are suggested as possible dynamics in the eventual development of independent illness
falsification behaviors. CONCLUSIONS: The many unanswered questions in our understanding of the development of factitious illness in children and adolescents suggest avenues for further research. It is hoped that increased understanding will eventually allow more rapid, reliable identification of these patients and more effective interventions within the family system, with positive implications for future generations.

PMID: 12079088 [PubMed - indexed for MEDLINE]

**Child Abuse Negl 2002 May;26(5):501-8**

**Different interpretations of Munchausen Syndrome by Proxy.**
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The definition of Munchausen Syndrome by Proxy is reviewed and considered in the context of the overlap with other harmful behaviors of parents. The high incidence of personal abnormal illness behavior in the perpetrators is leading to increasing concern about the safety of children who are cared for by parents who have abnormal illness behavior.

**Gen Hosp Psychiatry 2002 May-Jun;24(3):164-71**

**Factitious disorders and pathological self-harm in a hospital population: an interdisciplinary challenge.**
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Factitious disorder, Munchausen's Syndrome, and deliberate self-harm have recently been conceptualized as different facets of self-destructive behavior. A descriptive typological classification has been presented by Willenberg et al., but has not yet been tested with a clinical sample. The instrument distinguishes between direct self-harm (e.g., self-inflicted wounds), self-induced disease (e.g., factitious fever), and indirect self-harm delegated to medical staff (e.g., repeated operations occasioned by feigned symptoms). All patients referred to the psychosomatic-psychotherapeutic liaison-consultation service or to the outpatients' department within 14 months (n = 995) and all patients discharged from in-patient psychosomatic-psychotherapeutic treatment within 2 months (n = 62) were assessed. Expert instruction and supervision were provided for the diagnosticians. The assessment was continued for a subsequent year, without special supervision (n = 1,058). Self-destructive behaviors were diagnosed in 7.5% of the cases in the first sample, with certainty (59.5%) or on suspicion (40.5%). In the subsequent sample without supervision, the rate reduced to 3.6%. Referrals had come from almost all clinical departments, including the emergency unit (26%), surgery, internal intensive care, endocrinology (9.5% each), neurology, infectiology, nephrology (7.1% each), dermatology, gastro-enterology, cardiology (4.8% each) and surgical intensive care (2.4%). The occurrence of pathological self-destructive phenomena is underrated when using only the ICD-criteria. The rate is influenced by diagnostic attention.

PMID: 12062141 [PubMed - indexed for MEDLINE]

**Child Maltreat 2002 May;7(2):112-24**
Forensic assessment of illness falsification, Munchausen by proxy, and factitious disorder, NOS.
Sanders MJ, Bursch B.
Division of Child Psychiatry at Stanford University Medical School, USA.

The purpose of this article is to propose guidelines for the evaluation of possible Munchausen by proxy child abuse for the court systems. These assessments require the evaluator to have an understanding of the complexity involved when this type of abuse is alleged. The evaluator should have an appreciation of how falsification of illness may or may not occur, recognize the need for careful analysis of medical records, and understand the problems associated with the use of a profile in determining the validity of an abuse allegation. This article presents guidelines for gathering pertinent data, analyzing records, and evaluating psychological testing for forensic evaluations when the questions for the evaluation are the following: (a) Is there evidence that child abuse did occur? (b) Does the alleged perpetrator meet criteria for factitious disorder, NOS (or factitious disorder by proxy)? and (c) What management and treatment recommendations should be made?

Compr Psychiatry 2001 Jul-Aug;42(4):342-8

Is there a false memory syndrome? A review of three cases.
Kaplan R, Manicavasagar V.
Liaison Clinic, Wollongong, Australia.
The controversy over recovered memories of childhood sexual abuse (CSA) is whether such experiences can be forgotten for long periods and retrieved later in therapy or in response to cues or triggers from the environment. False memory syndrome (FMS) is caused by memories of a traumatic experience--most frequently CSA--which are objectively false, but in which the person strongly believes. Personality factors often play a role in the development of FMS. Because CSA is such a devastating experience, false accusations of sexual abuse have enormous, if not shattering, consequences for families. We present three case reports to illustrate features of the FMS. FMS should be listed for further study to establish valid criteria for making the diagnosis under the category of "factitious disorders," and a subcategory of "false memories/beliefs of abuse," with a further subdivision of "induced by therapy." The FMS controversy occurred in the context of a general moral panic about sexual abuse in the early 1980s. Psychiatrists should have a high degree of scepticism to moral panics.

Urology 2002 Apr;59(4):601

Munchausen syndrome presenting as gross hematuria in two women.
Chew BH, Pace KT, Honey RJ.
Division of Urology, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada.
Munchausen syndrome is an uncommon disorder in which patients present with fictitious disorders and a self-destructive urge to undergo invasive procedures. We present 2 cases of nurses who presented with recurrent urinary tract infections, flank pain, and gross hematuria. One patient had such severe hematuria as to require transfusions of more than 1000 U of packed red cells during a 30-year period. Both patients underwent extensive investigations--all of which were normal. One patient even underwent nephrectomy, which showed normal pathologic
findings. Both were found to be phlebotomizing themselves and infusing blood into their bladders.

Med Leg J 2002;70(Pt 1):38-49
Recent research into dealing with the problem of malingering.
Lowenstein LF.
Publication Types: Review

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Structural and energetic processes related to P300: LORETA findings in depression and effects of antidepressant drugs.
Anderer P, Saletu B, Semlitsch HV, Pascual-Marqui RD.
Section of Sleep Research and Pharmacopsychiatry, Department of Psychiatry, University of Vienna, Vienna, Austria. peter.anderer@akh-wien.ac.at
Noninvasive electrophysiological neuroimaging applied to cognitive components of event-related potentials (ERPs) may differentiate between structural and energetic processes related to information processing. The structural level, revealed by the location of the local maxima of the current source density distribution, describes the time-dependent network of activated brain areas. The magnitude of the source strength, a measure of the energetic component, describes the allocation of processing resources. ERPs were recorded in an odd-ball paradigm and low-resolution brain electromagnetic tomography (LORETA) was applied for standard and target ERP components. In a group of 60 menopausal depressed patients of 45-60 years of age, reduced P300 source strength was observed bilaterally, temporally and medially prefrontally reaching to rostral parts of the anterior cingulate, compared with 29 age-matched controls. In a double-blind, placebo-controlled study, 2 mg of the antidepressant citalopram induced a significant increase of P300 source strength in the (left) prefrontal cortex and precuneus compared with placebo, reaching to the posterior cingulate. Similar increases were observed after 800 mg S-adenosyl-L-methionine (SAMe) administered intravenously in ten young healthy subjects aged 22-33, and they were even more pronounced in ten elderly healthy subjects aged 56-71. Thus, ERP-tomography identified changes in energetic sources in brain areas predominantly involved in depression and in antidepressant action.

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**Smell Sensitivity May Be Reduced in Depression**

By Hannah Cleaver

BERLIN (Reuters Health) Feb 07 - People with serious depression seem to have an impaired ability to smell faint odours, German researchers have found. Their discovery strengthens indications that olfactory function and mood interact in some way.

Dr. Bettina Pause and colleagues at Kiel University examined subjective and objective indications of smell acuity in depressed patients being treated in hospital, and compared the results with a control group of non-depressed subjects.

"Compared to the control group they only began to perceive smells at higher concentrations," she told Reuters Health. Depressive patients could not perceive very weak smells at all, at concentrations where the control group did smell them.

"We also conducted the tests using EEG to give an objective check, and found the same reduced sensitivity when compared to non-depressives; their brains reacted later and only to stronger smells," said Dr. Pause.

Her latest study is due to be published in the journal Psychophysiology in March. It involved just over 20 depressive patients and a similar number of non-depressives.

"This is the third such study we have conducted," she said. "The results are the same and show a clear association between depression and reduced sensitivity to smell."
Cause and effect do not seem likely in either direction, and Dr. Pause is looking for an explanation for the association. "A clue could be that the area of the brain responsible for smell and that for emotions are parallel; they may even be almost identical."

Dr. Pause said the work could lead to the use of smell tests to confirm a diagnosis of depression, or even as a first diagnostic tool in the case of people with communication difficulties. In this study, smell sensitivity was not affected by the nature of the odour used in the tests, but Dr. Pause is also working on further experiments examining olfactory perception in people suffering schizophrenia. Previous studies of schizophrenics have shown that they have confused perceptions of smell, reacting strongly to unpleasant smells but often not appreciating pleasant ones.

Other work involving people with seasonal affective disorder (SAD) has shown they have a more acute sense of smell than those without the condition, adding to the growing body of evidence of a link between olfactory function and mental status.

Reduced olfactory performance in patients with major depression.
Pause BM, Miranda A, Goder R, Aldenhoff JB, Ferstl R.
Department of Psychology, Christian-Albrechts-University of Kiel, Olshausenstr. 62, 24098, Kiel, Germany. bmpause@psychologie.uni-kiel.de

The aim of the present study is to investigate olfactory sensitivity and odor evaluations in a homogeneous sample of unipolar depressive patients using pure olfactory odors. Twenty-four in-patients with major depressive disorder (MDD) were investigated during their acute depressive phase. Eighteen of them participated a second time after successful treatment. A group of healthy subjects, matched by age, sex, and smoking behavior, served as a control. Olfactory sensitivity, as measured by threshold tests, was strongly reduced in patients with severe depression. Additional correlative analyses revealed that the lowered sensitivity could partly be predicted by high depression scores. After successful medical treatment, these sensitivity differences were reduced and did not reach the significance level. The subjective odor evaluations (valence and intensity ratings) were not markedly changed in general. The results reveal that olfactory performance in MDD patients is reduced at an early perceptual level of stimulus processing. It is discussed whether this effect can be attributed to the close functional connection between the main olfactory bulb and the amygdala.

Arch Gen Psychiatry 2002 Dec;59(12):1119-22
Patients with seasonal affective disorder have lower odor detection thresholds than control subjects.
Postolache TT, Wehr TA, Doty RL, Sher L, Turner EH, Bartko JJ, Rosenthal NE.
BACKGROUND: Behavioral changes in patients with seasonal affective disorder resemble seasonal changes in photoperiodic animals. Because the olfactory system has a modulatory role in seasonal photoperiodic responses in certain species, we hypothesized that olfactory function may differ between patients with seasonal affective disorder and healthy control subjects.

METHODS: Fourteen patients who had winter seasonal affective disorder and 16 healthy volunteers were studied once in winter and once in the subsequent summer. We administered a phenyl ethyl alcohol detection threshold test to each side of the nose in a counterbalanced order, with the nostril contralateral to the tested site occluded. Patient and control data were compared using a 4-way repeated measure analysis of covariance (with group and gender as between-subjects factors, season and side-of-the-nose as within-subjects factors, and age as a covariate).

RESULTS: The patients exhibited lower thresholds than did the controls ($F(1,25) = 9.2; P = .006$). There was no main effect of season.

CONCLUSION: In humans, marked seasonal behavioral rhythms with recurrent winter depression may be associated with a more acute sense of smell.


Reduced olfactory performance in patients with major depression.
Pause BM, Miranda A, Goder R, Aldenhoff JB, Ferstl R.
Department of Psychology, Christian-Albrechts-University of Kiel, Olshausenstr. 62, 24098, Kiel, Germany. bmpause@psychologie.uni-kiel.de

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Dev Psychobiol 2003 Mar;42(2):171-80

Olfactory experience mediates response to pain in preterm newborns.
Goubet N, Rattaz C, Pierrat V, Bullinger A, Lequien P.
Department of Psychology, Gettysburg College, Gettysburg, PA 17325.
We assessed the effects of a familiar odor during routine blood draws in healthy preterm newborns. Infants were observed as they were undergoing either a capillary puncture on the heel (heelstick) or a venous puncture on the hand. During the procedure, one third of the infants were
presented with an odor they had been familiarized with prior to the procedure, one third of the
infants were presented with an odor, they had not been previously exposed to, and one third were
presented with no odor. Heelsticks elicited more behavioral distress than venipunctures. **Infants**
who were presented with a familiar odor during venipuncture showed no significant
increase in crying and grimacing during the procedure compared to baseline levels. By
comparison, infants presented with an unfamiliar odor or with no odor either during the
heelstick or the venipuncture had a significant increase in crying and grimacing. When the
pain was milder, i.e., during a venipuncture, and a familiar odor was presented, infants showed
little to no crying. **These results are consistent with a body of evidence on early memory and
olfactory competence in fetuses and newborns.**

**Mult Scler 2000 Dec;6(6):386-90**

**Olfactory dysfunction and extent of white matter abnormalities in multiple sclerosis: a
clinical and MR study.**
Neurological Clinic, University of Trieste, Italy.

**BACKGROUND:** The relative contribution to the olfactory dysfunction of the lesions in
the specific brain regions involved in olfaction compared with the lesions scattered all over the
rest of the brain has not been fully clarified yet in patients with multiple sclerosis (MS). The
concurrent use of Magnetic Resonance Imaging (MRI) and a standardized test of odor
identification ability now permits to study the relation between smell loss and the extent of white
matter abnormalities. **METHODS:** We tested the olfactory function of 40 patients with definite
MS and of 40 age-sex- and smoking-habit-matched healthy controls by using the Cross Cultural
Smell Identification Test. We measured also the lesion load on T2-weighted images in the
inferior-frontal and temporal lobes and in the rest of the brain in MS patients. Therefore, we tried
to correlate measures of lesion load and smell test scores. **RESULTS:** A robust correlation was
demonstrated between MR measures of lesion load in the white matter of the olfactory brain
region and smell loss (r=-0.739, P<0.0001). A significant relationship has been found even after
taking potential confounding factors, such as sex, age, disease duration, disability, anxiety and
depression, into account (r=-0.90, P<0.0001). **CONCLUSIONS:** Our findings show, in MS
patients with stable neurological impairment and no recent disease exacerbation, a correlation
between smell loss and the lesion load in the regions of the brain involved in olfaction and
support the theory that the extent and severity of MRI abnormalities in specific brain regions are
related to the presence of selective neurologic and neuropsychologic impairment.

**Nervenarzt 2002 Jan;73(1):71-7**

**[Evaluation of olfactory stimuli by depressed patients]**
[Article in German]
Thomas HJ, Fries W, Distel H.
Institut fur Medizinische Psychologie, Ludwig-Maximilians-Universitat Munchen.

Anhedonia, a cardinal sign of depression, is discussed to originate from a
transmitter dysbalance in the central dopaminergic reward system. This system involves
neuroanatomically many structures of the olfactory system. Hence the question arises whether anhedonia can be quantified when depressive patients judge smells hedonically. Sensory evaluation of olfactory stimuli by 16 depressive patients was compared that of an age-matched control group. In the group comparison, mono- and birhinal sensory thresholds as well as judgment of intensity were not significantly different. For four of the eight smells, the hedonic judgements were found to be identical between the group of depressives and controls, with the remaining smells not significantly different. There were no differences in the consistency of ranking of smells. In a longitudinal (test-retest) assessment there were again no differences in intensity, familiarity, and hedonic quality of the smells. The findings suggest that changes in the dopaminergic transmitter balance during the state of depression causing anhedonia affect neither olfactory perception nor the hedonic judgement of smells. Contrary to the clinical picture, anhedonia thus seems not to arise at the level of sensory perception yet but should be considered a more complex construct of disturbed central processing.

Affect Disord 1999 Nov;56(1):27-35
Monorhinal odor identification and depression scores in patients with seasonal affective disorder.
Section on Biological Rhythms/NIMH, Bethesda, MD 20892-1390, USA. postolache@nih.gov
BACKGROUND: Visual and olfactory pathways are interconnected. Olfactory deafferentation unmasks photoperiodic responsiveness in some nonphotoperiodic animals such as laboratory rats. By analogy, we hypothesized that olfactory deficits may unmask seasonal rhythms in certain individuals, namely those with seasonal affective disorder (SAD). Since previous studies suggest lateralized hemispheric dysfunction in SAD, and since olfactory neurons' primary projections are largely ipsilateral, we assessed olfactory identification performance on both the right and left side of the nose. METHODS: Twenty-four patients with SAD and 24 matched controls were studied using a phenyl ethyl alcohol detection threshold test bilaterally and the University of Pennsylvania Smell Identification Test unilaterally. Subjects rated their mood using the Self Assessment Mood Scale for SAD. Patients' testing was done in both 'depressed' and 'improved on light' states. RESULTS: No difference in olfactory performance was found between patients and controls or between patients before and after light treatment. However, right-side identification scores were negatively correlated with 'typical' depression scores (r = -0.56, P = 0.006), while left-side olfactory scores were not. Atypical depression scores were unrelated to olfactory performance. Similar correlations emerged between the olfactory identification laterality quotient (Right - Left)/(Right + Left) and typical depressive scores (r = -0.64, P < 0.001) and total depression scores (r = -0.59, P < 0.004). LIMITATIONS: We studied a demographically heterogeneous sample and did not control for menstrual factors. DISCUSSION: Our results add to previous evidence of lateralized hemispheric involvement in SAD and suggest that olfaction may be related to seasonal emotional rhythms in humans.

Neurophysiol Clin 2002 Dec;32(6):335-42
Modulation of visual event-related potentials by emotional olfactory stimuli.
The objective of the present study was to determine whether an olfactory prime could
telegraph behavior and visual event-related potentials (ERPs) obtained in response to a visual
stimulation representing female faces. More specifically, we tested the hypothesis that a pleasant
odor could have effects on face perception: behavioral effects on subjective emotional estimation
of faces, and on associated response times, and electrophysiological effects on the N400 and late
positive complex or LPC. Experiments were performed in which subjects had to decide whether
the presented face was pleasant or not, while visual ERPs were recorded. Faces were always
primed with either a pleasant odor or a neutral olfactory stimulus (pure air). In order to test the
effect of subject's awareness, participants were not informed that an odor would be presented in
the experimental sessions. Responses were significantly shorter for unpleasant faces. However,
no behavioral effects of the pleasant odor on response time or on evaluation of face pleasantness
were observed. Late ERPs evoked by faces were modulated by the presence of a pleasant
odor, even when subjects were neither warned nor aware of the presence of the odor: in a
frontal site and after the diffusion of the odor, the LPC (appearing 550 ms after the
presentation of the visual stimulus) evoked by unpleasant faces was significantly more
positive than the LPC evoked by pleasant faces. This effect could reflect an enhanced alert
reaction to unpleasant faces are preceded by an (incongruous) pleasant odor.

Evidence of conscious and subconscious olfactory information processing during word
encoding: a magnetoencephalographic (MEG) study.
Department for Clinical Neurology, Wahringer Gurtel 18-20, A-1090, Vienna, Austria.
peter.walla@akh-wien.ac.at

The present study was meant to distinguish between unconscious and conscious olfactory
information processing and to investigate the influence of olfaction on word information
processing. Magnetic field changes were recorded in healthy young participants during deep
encoding of visually presented words whereby some of the words were randomly associated with
an odor. All recorded data were then split into two groups. One group consisted of participants
who did not consciously perceive the odor during the whole experiment whereas the other group
did report continuous conscious odor perception. The magnetic field changes related to the
condition 'words without odor' were subtracted from the magnetic field changes related to the
condition 'words with odor' for both groups. First, an odor-induced effect occurred between
about 200 and 500 ms after stimulus onset which was similar in both groups. It is interpreted to
reflect an activity reduction during word encoding related to the additional olfactory stimulation.
Second, a later effect occurred between about 600 and 900 ms after stimulus onset which
differed between the two groups. This effect was due to higher brain activity related to the
additional olfactory stimulation. It was more pronounced in the group consisting of participants
who consciously perceived the odor during the whole experiment as compared to the other
group. These results are interpreted as evidence that the later effect is related to conscious
odor perception whereas the earlier effect reflects unconscious olfactory information.
processing. Furthermore, our study provides evidence that only the conscious perception of an odor which is simultaneously presented to the visual presentation of a word reduces its chance to be subsequently recognized.

Chem Senses 2002 Oct;27(8):703-9

**Autonomic nervous system responses to odours: the role of pleasantness and arousal.**

Bensafi M, Rouby C, Farget V, Bertrand B, Vigouroux M, Holley A.

Laboratoire de Neurosciences et Systemes Sensoriels CNRS UMR 5020 and Universite Claude Bernard Lyon 1, 50 avenue Tony Garnier, 69366 Lyon Cedex 07, France. bensafi@olfac.univ-lyon1.fr

Perception of odours can provoke explicit reactions such as judgements of intensity or pleasantness, and implicit output such as skin conductance or heart rate variations. The main purpose of the present experiment was to ascertain: (i) the correlation between odour ratings (intensity, arousal, pleasantness and familiarity) and activation of the autonomic nervous system, and (ii) the inter-correlation between self-report ratings on intensity, arousal, pleasantness and familiarity dimensions in odour perception. Twelve healthy volunteers were tested in two separate sessions. Firstly, subjects were instructed to smell six odorants (isovaleric acid, thiophenol, pyridine, L-menthol, isoamyl acetate, and 1-8 cineole), while skin conductance and heart rate variations were being measured. During this phase, participants were not asked to give any judgement about the odorants. Secondly, subjects were instructed to rate the odorants on dimensions of intensity, pleasantness, arousal and familiarity (self-report ratings), by giving a mark between 1 (not at all intense, arousing, pleasant or familiar) and 9 (extremely intense, arousing, pleasant or familiar). Results indicated: (i) a pleasantness factor correlated with heart rate variations, (ii) an arousal factor correlated with skin conductance variations, and (iii) a strong correlation between the arousal and intensity dimensions. In conclusion, given that these correlations are also found in other studies using visual and auditory stimuli, these findings provide preliminary information suggesting that autonomic variations in response to olfactory stimuli are probably not modality specific, and may be organized along two main dimensions of pleasantness and arousal, at least for the parameters considered (i.e. heart rate and skin conductance).

Brain Res 2002 Sep 27;951(1):77-81

**Olfactory identification and apolipoprotein E epsilon 4 allele in mild cognitive impairment.**

Wang QS, Tian L, Huang YL, Qin S, He LQ, Zhou JN.

Laboratory of Neurodegenerative Diseases, School of Life Science, University of Science and Technology of China, 230027, Hefei, PR China.

To investigate olfactory identification and apolipoprotein E epsilon 4 allele in patients with mild cognitive impairment (MCI), we used Cross-Cultural Smell Identification Test (CC-SIT) from University of Pennsylvania to assess olfactory identification performance and polymerase chain reaction (PCR) to detect apolipoprotein E epsilon 4 (ApoE epsilon 4) allele in 28 patients with MCI and the 30 age-matched control subjects in present study. The Mann-Whitney U test demonstrated that the MCI group performed significantly worse on CC-SIT than
the normal aging group (P<0.01). For MCI patients olfaction scores correlated positively with CAMCOG-C (r=0.61, P<0.01), but not with age, gender or years of education. In normal subjects, the CC-SIT score showed no significant associations with age, gender, years of education, or CAMCOG-C. As the least common allele in Chinese, epsilon 4 was found in 13.3% of controls and in 35.8% of MCI in this study. ApoE epsilon 4 was significantly higher in MCI group than normal group (chi(2)=4.65, P<0.01). There was a significant effect of allele status on odor identification: subjects with epsilon 4 allele were not able to identify as many odors as the subjects without epsilon 4 allele (P<0.01). These results suggested that the decreased olfactory identification in MCI may be a marker for the early diagnosis of Alzheimer's disease, and ApoE genotype may be part of the basis of olfactory identification decline.

Nat Rev Neurosci 2002 Jul;3(7):563-73

The amygdala and reward.

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The amygdala -- an almond-shaped group of nuclei at the heart of the telencephalon -- has been associated with a range of cognitive functions, including emotion, learning, memory, attention and perception. Most current views of amygdala function emphasize its role in negative emotions, such as fear, and in linking negative emotions with other aspects of cognition, such as learning and memory. However, recent evidence supports a role for the amygdala in processing positive emotions as well as negative ones, including learning about the beneficial biological value of stimuli. Indeed, the amygdala's role in stimulus-reward learning might be just as important as its role in processing negative affect and fear conditioning.

Neurobiol Aging 2002 May-Jun;23(3):397-404

Taste, smell and neuropsychological performance of individuals at familial risk for Alzheimer's disease.

Schiffman SS, Graham BG, Sattely-Miller EA, Zervakis J, Welsh-Bohmer K.
Department of Psychiatry, Duke University Medical Center, Durham, NC 27710, USA. sss@duke.edu

The purpose of the study was to determine whether there are chemosensory and neuropsychological changes that predate the onset of Alzheimer's disease in individuals at enhanced risk of developing the condition. To study this question, a unique sample of individuals (n = 33) was studied who were genetically at-risk for AD by virtue of documented multigenerational evidence of the disease (so-called multiplex families). The performance of at-risk individuals was evaluated on various smell, taste, and neuropsychological measures at baseline and 18 months later. Their performance was compared to a control group (n = 32) that was matched in age, gender, education, and race. At baseline the at-risk group performed worse than the control group on the chemosensory measures of phenethyl alcohol smell detection, smell memory, and taste memory, and on a memory measure involving recall of narrative information (Logical Memory I from the Wechsler Memory Scale- Revised). Across both sessions, the at-risk
group had lower smell memory scores than the control group. At-risk status was not significantly associated with APOE status. The results of this and other studies suggest that individuals who are genetically at risk for developing AD may perform more poorly on memory and smell measures compared to those not at risk. This effect may be separate from one known genetic risk factor of AD, APOE, and supports that multiple genes are likely responsible for the disease and its associated memory and other neurocognitive symptoms.


Apolipoprotein E status is associated with odor identification deficits in nondemented older persons.
Murphy C, Bacon AW, Bondi MW, Salmon DP.
University of California, San Diego, La Jolla 92093-0957, USA. cmurphy@sunstroke.sdsu.edu

Alzheimer's disease (AD) patients with moderate dementia show losses in olfactory threshold, odor identification and odor memory. Sensitivity and specificity of olfactory testing is significant, with the greatest power of accurate diagnosis in the more cognitively loaded olfactory tasks. In patients with very mild AD or in patients at risk for the disease because of their mild cognitive impairment, losses are apparent for odor identification, odor recognition memory and odor threshold, with the best sensitivity in the identification task. Persons who are either heterozygous or homozygous for the epsilon 4 allele of apolipoprotein E (ApoE) have an increased risk of Alzheimer's disease, although they show no dementia in the preclinical period. Evidence of olfactory dysfunction in this population might be reflective of an incipient dementing process. We have recently examined olfactory function in a group of normal elderly persons who have undergone genetic testing for the Apoe4 allele. These individuals consisted of all normal control subjects at the University of California, San Diego (UCSD) Alzheimer's Disease Research Center (ADRC) who had undergone both the genetic testing and testing for olfactory function. All had been diagnosed as normal control participants by two different neurologists who applied the National Institute of Neurological Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINDS-ADRDA) criteria for dementia. Persons with a history of alcoholism, drug abuse, learning disability or neurologic or psychiatric illness (including depression) were excluded. In this population, persons with the Apoe4 allele showed significantly poorer odor identification than those without an epsilon 4 allele. Early appearance of olfactory deficits in the progression to AD in persons with the epsilon 4 allele suggests diagnostic utility in olfactory testing.

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CONTINUES BELOW, in other TOPIC AREAS...

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The Journal of Neuropsychiatry and Clinical Neurosciences 2002; 14:197–201
The Pocket Smell Test: Successfully Discriminating Probable Alzheimer’s Dementia From Vascular Dementia and Major Depression.

Kevin Duff, Ph.D., Robert J. McCaffrey, Ph.D., Gary S. Solomon, Ph.D.

The present study extended previous work on olfactory dysfunction (odor identification deficits) by using the Pocket Smell Test (PST) to discriminate between groups of patients with Alzheimer’s disease (AD), vascular dementia (VaD), and major depression (MD). Sixty patients meeting the DSM-IV criteria for either AD, VaD, or MD (20 per group) underwent assessment with the PST, a three-item screening measure of odor identification, and the Mini-Mental State Examination (MMSE). Patients with AD scored significantly lower than patients with either VaD or MD on the PST, even after controlling for MMSE scores. A PST score of 1 (i.e., 1 or 0 correct) discriminated between patients with and without AD with a classification accuracy of 95% (sensitivity 100%, specificity 92.5%). Olfactory assessment may be of diagnostic utility in the differential diagnosis of AD versus VaD versus MD in elderly patients.


Olfactory Dysfunction Discriminates Alzheimer’s Dementia From Major Depression. Gary S. Solomon, Ph.D. William M. Petrie, M.D., James R. Hart, M.D., Henry B. Brackin, Jr., M.D.

This study tested the hypothesis that olfactory dysfunction could discriminate between groups of patients with Alzheimer’s disease and major depression. Forty patients meeting DSM-IV criteria for Alzheimer’s disease and for major depression (20 per group) underwent assessment with the Pocket Smell Test (PST), a three-item screening measure of cranial nerve I function. A PST score of #1 (1 or 0 correct) discriminated between the groups with a hit rate of 90% (sensitivity 480%, specificity 4100%). Olfactory assessment may be a useful adjunctive screening measure in differentiating Alzheimer’s disease from depression in elderly patients.

The Journal of Neurology Neurosurgery and Psychiatry 2002;73:672-677

The apolipoprotein E 2 allele and decline in episodic memory

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Objectives: The apolipoprotein E (apoE) 4 allele is related to decline in multiple cognitive domains, especially episodic memory, but the effect of the 2 allele on change in different forms of cognitive function has been difficult to establish.

Methods: Participants are from the Religious Orders Study. At baseline, they were at least 65 years old and free of clinical evidence of dementia. For up to eight years, they underwent annual clinical evaluations that included detailed cognitive function assessment from which previously established summary measures of episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability were derived. Growth curve models were used to assess change in each measure and its relation to apoE genotype, controlling for age, sex, education, and baseline level of cognition. Follow up data were available in 669 persons (98% of those eligible). We treated those with the 3/3 genotype as the reference group (n=425), which was contrasted with 2 (2/2, 2/3; n=86), and 4 (3/4, 4/4; n=158) subgroups.

Results: Rate of episodic memory change in the three subgroups significantly differed, with an average annual increase of 0.016 units in the 2 subgroup and annual decreases of 0.022 units in
Conclusion: Possession of one or more apoE 2 alleles is associated with reduced decline in episodic memory in older persons.

Olfactory dysfunction discriminates probable Alzheimer's dementia from major depression: a cross-validation and extension.
McCaffrey RJ, Duff K, Solomon GS.
University at Albany-State University of New York and Psychiatric Consultants, PC, USA.
The present study was conducted to cross-validate and extend the hypothesis that olfactory dysfunction could discriminate between groups of patients with Alzheimer's disease and major depression. Forty patients meeting the DSM-IV criteria for either Alzheimer's disease or major depression (20 per group) underwent assessment with the Pocket Smell Test (PST), a three-item screening measure of odor identification, and the Mini-Mental State Examination (MMSE). A PST score of \( \leq 1 \) (1 or 0 correct) discriminated between the groups with a hit rate of 97.5% (sensitivity = 95%, specificity = 100%). The optimal hit rate for the MMSE (< or =24) was less effective (hit rate = 90%, sensitivity = 80%, specificity = 100%). Age, gender, and education had minimal impact on the PST for both groups. Olfactory assessment continues to add to the diagnostic utility in the differential diagnosis of Alzheimer's disease versus major depression in elderly patients.

Olfaction in neurodegenerative disorder.
Hawkes C.
Essex Centre for Neuroscience, Oldchurch Hospital, Romford, Essex, United Kingdom.
There has been an increase of interest in olfactory dysfunction since it was realised that anosmia was a common feature of idiopathic Parkinson's disease (PD) and Alzheimer-type dementia (AD). It is an intriguing possibility that the first sign of a disorder hitherto regarded as one of movement or cognition may be that of disturbed smell sense. In this review of PD, parkinsonian syndromes, essential tremor, AD, motor neurone disease (MND) and Huntington's chorea (HC) the following observations are made: 1) olfactory dysfunction is frequent and often severe in PD and AD; 2) normal smell identification in PD is rare and should prompt review of diagnosis unless the patient is female with tremor-dominant disease; 3) anosmia in suspected progressive supranuclear palsy and corticobasal degeneration is atypical and should likewise provoke diagnostic review; 4) hyposmia is an early feature of PD and AD and may precede motor and cognitive signs respectively; 5) subjects with anosmia and one ApoE-4 allele have an approximate 5-fold increased risk of later AD; 6) impaired smell sense is seen in some patients at 50% risk of parkinsonism; 7) smell testing in HC and MND where abnormality may be found, is not likely to be of clinical value; and 8) biopsy of olfactory nasal neurons shows non-specific changes in PD and AD and at present will not aid diagnosis.
Aromas of rosemary and lavender essential oils differentially affect cognition and mood in healthy adults.

Moss M, Cook J, Wesnes K, Duckett P.

Human Cognitive Neuroscience Unit, Division of Psychology, Northumberland Building, University of Northumbria, Newcastle upon Tyne, NE1 8ST, UK. mark.moss@unn.ac.uk

This study was designed to assess the olfactory impact of the essential oils of lavender (Lavandula angustifolia) and rosemary (Rosmarinus officinalis) on cognitive performance and mood in healthy volunteers. One hundred and forty-four participants were randomly assigned to one of three independent groups, and subsequently performed the Cognitive Drug Research (CDR) computerized cognitive assessment battery in a cubicle containing either one of the two odors or no odor (control). Visual analogue mood questionnaires were completed prior to exposure to the odor, and subsequently after completion of the test battery. The participants were deceived as to the genuine aim of the study until the completion of testing to prevent expectancy effects from possibly influencing the data. The outcome variables from the nine tasks that constitute the CDR core battery feed into six factors that represent different aspects of cognitive functioning. Analysis of performance revealed that lavender produced a significant decrement in performance of working memory, and impaired reaction times for both memory and attention based tasks compared to controls. In contrast, rosemary produced a significant enhancement of performance for overall quality of memory and secondary memory factors, but also produced an impairment of speed of memory compared to controls. With regard to mood, comparisons of the change in ratings from baseline to post-test revealed that following the completion of the cognitive assessment battery, both the control and lavender groups were significantly less alert than the rosemary condition; however, the control group was significantly less content than both rosemary and lavender conditions. These findings indicate that the olfactory properties of these essential oils can produce objective effects on cognitive performance, as well as subjective effects on mood.

Neurophysiol Clin 2002 Dec;32(6):335-42

Modulation of visual event-related potentials by emotional olfactory stimuli.

Laboratoire de neurosciences et systemes sensoriels, CNRS et Universite Claude Bernard Lyon 1, 50, avenue Tony Garnier, 69366 Lyon cedex 7, France. bensafi@olfac.univ-lyon1.fr

The objective of the present study was to determine whether an olfactory prime could modulate behavior and visual event-related potentials (ERPs) obtained in response to a visual stimulation representing female faces. More specifically, we tested the hypothesis that a pleasant odor could have effects on face perception: behavioral effects on subjective emotional estimation of faces, and on associated response times, and electrophysiological effects on the N400 and late positive complex or LPC. Experiments were performed in which subjects had to decide whether the presented face was pleasant or not, while visual ERPs were recorded. Faces were always primed with either a pleasant odor or a neutral olfactory stimulus (pure air). In order to test the effect of subject's awareness, participants were not informed that an odor would be presented in the experimental sessions. Responses were significantly shorter for unpleasant faces. However,
no behavioral effects of the pleasant odor on response time or on evaluation of face pleasantness were observed. Late ERPs evoked by faces were modulated by the presence of a pleasant odor, even when subjects were neither warned nor aware of the presence of the odor: in a frontal site and after the diffusion of the odor, the LPC (appearing 550 ms after the presentation of the visual stimulus) evoked by unpleasant faces was significantly more positive than the LPC evoked by pleasant faces. This effect could reflect an enhanced alert reaction to unpleasant faces are preceded by an (incongruous) pleasant odor.

Brain Res Cogn Brain Res 2002 Nov;14(3):309-16
Evidence of conscious and subconscious olfactory information processing during word encoding: a magnetoencephalographic (MEG) study.
Department for Clinical Neurology, Wahringer Gurtel 18-20, A-1090, Vienna, Austria.
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The present study was meant to distinguish between unconscious and conscious olfactory information processing and to investigate the influence of olfaction on word information processing. Magnetic field changes were recorded in healthy young participants during deep encoding of visually presented words whereby some of the words were randomly associated with an odor. All recorded data were then split into two groups. One group consisted of participants who did not consciously perceive the odor during the whole experiment whereas the other group did report continuous conscious odor perception. The magnetic field changes related to the condition 'words without odor' were subtracted from the magnetic field changes related to the condition 'words with odor' for both groups. First, an odor-induced effect occurred between about 200 and 500 ms after stimulus onset which was similar in both groups. It is interpreted to reflect an activity reduction during word encoding related to the additional olfactory stimulation. Second, a later effect occurred between about 600 and 900 ms after stimulus onset which differed between the two groups. This effect was due to higher brain activity related to the additional olfactory stimulation. It was more pronounced in the group consisting of participants who consciously perceived the odor during the whole experiment as compared to the other group. These results are interpreted as evidence that the later effect is related to conscious odor perception whereas the earlier effect reflects unconscious olfactory information processing. Furthermore, our study provides evidence that only the conscious perception of an odor which is simultaneously presented to the visual presentation of a word reduces its chance to be subsequently recognized.

Chem Senses 2002 Oct;27(8):703-9
Autonomic nervous system responses to odours: the role of pleasantness and arousal.
Bensafi M, Rouby C, Farget V, Bertrand B, Vigouroux M, Holley A.
Laboratoire de Neurosciences et Systemes Sensoriels CNRS UMR 5020 and Universite Claude Bernard Lyon 1, 50 avenue Tony Garnier, 69366 Lyon Cedex 07, France. bensafi@olfac.univ-lyon1.fr
Perception of odours can provoke explicit reactions such as judgements of intensity or pleasantness, and implicit output such as skin conductance or heart rate variations. The main purpose of the present experiment was to ascertain: (i) the correlation between odour ratings (intensity, arousal, pleasantness and familiarity) and activation of the autonomic nervous system, and (ii) the inter-correlation between self-report ratings on intensity, arousal, pleasantness and familiarity dimensions in odour perception. Twelve healthy volunteers were tested in two separate sessions. Firstly, subjects were instructed to smell six odorants (isovaleric acid, thiophenol, pyridine, L-menthol, isoamyl acetate, and 1-8 cineole), while skin conductance and heart rate variations were being measured. During this phase, participants were not asked to give any judgement about the odorants. Secondly, subjects were instructed to rate the odorants on dimensions of intensity, pleasantness, arousal and familiarity (self-report ratings), by giving a mark between 1 (not at all intense, arousing, pleasant or familiar) and 9 (extremely intense, arousing, pleasant or familiar). Results indicated: (i) a pleasantness factor correlated with heart rate variations, (ii) an arousal factor correlated with skin conductance variations, and (iii) a strong correlation between the arousal and intensity dimensions. In conclusion, given that these correlations are also found in other studies using visual and auditory stimuli, these findings provide preliminary information suggesting that autonomic variations in response to olfactory stimuli are probably not modality specific, and may be organized along two main dimensions of pleasantness and arousal, at least for the parameters considered (i.e. heart rate and skin conductance).

Brain Res 2002 Sep 27;951(1):77-81
Olfactory identification and apolipoprotein E epsilon 4 allele in mild cognitive impairment.
Wang QS, Tian L, Huang YL, Qin S, He LQ, Zhou JN.
Laboratory of Neurodegenerative Diseases, School of Life Science, University of Science and Technology of China, 230027, Hefei, PR China.

To investigate olfactory identification and apolipoprotein E epsilon 4 allele in patients with mild cognitive impairment (MCI), we used Cross-Cultural Smell Identification Test (CC-SIT) from University of Pennsylvania to assess olfactory identification performance and polymerase chain reaction (PCR) to detect apolipoprotein E epsilon 4 (ApoE epsilon 4) allele in 28 patients with MCI and the 30 age-matched control subjects in present study. The Mann-Whitney U test demonstrated that the MCI group performed significantly worse on CC-SIT than the normal aging group (P<0.01). For MCI patients olfaction scores correlated positively with CAMCOG-C (r=0.61, P<0.01), but not with age, gender or years of education. In normal subjects, the CC-SIT score showed no significant associations with age, gender, years of education, or CAMCOG-C. As the least common allele in Chinese, epsilon 4 was found in 13.3% of controls and in 35.8% of MCI in this study. ApoE epsilon 4 was significantly higher in MCI group than normal group (chi(2)=4.65, P<0.01). There was a significant effect of allele status on odor identification: subjects with epsilon 4 allele were not able to identify as many odors as the subjects without epsilon 4 allele (P<0.01). These results suggested that the decreased olfactory identification in MCI may be a marker for the early diagnosis of Alzheimer's disease, and ApoE genotype may be part of the basis of olfactory identification decline.
The amygdala -- an almond-shaped group of nuclei at the heart of the telencephalon -- has been associated with a range of cognitive functions, including emotion, learning, memory, attention and perception. Most current views of amygdala function emphasize its role in negative emotions, such as fear, and in linking negative emotions with other aspects of cognition, such as learning and memory. However, recent evidence supports a role for the amygdala in processing positive emotions as well as negative ones, including learning about the beneficial biological value of stimuli. Indeed, the amygdala's role in stimulus-reward learning might be just as important as its role in processing negative affect and fear conditioning.

Associations to smell are more pleasant than to sound.
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Department of Neurology, University Hospital Zurich, Switzerland. christine.mohr@nos.usz.ch

To assess and compare the quantitative and qualitative aspects of verbal associations of olfaction and audition, we conducted two verbal category fluency tasks, one consisting of the generation of 'smelling' associations and the other of 'auditory' associations. The responses of the 40 subjects on these fluency tasks were rated as pleasant or unpleasant by themselves as well as by an independent group of 40 subjects. In addition, all 80 healthy, right-handed subjects rated their momentary emotional state on a visual analog scale. The mean number of words generated by the 40 subjects did not differ between the two tasks, and in both tasks pleasant associations were more frequent than unpleasant associations. However, for all subjects, the proportion of pleasant associations was significantly higher in the olfactory compared to the auditory fluency task. The finding of more pleasant associations in both tasks confirms previous reports, but the pronounced effect in the olfactory task suggests that odors may be more hedonically coded than other sensory modalities, i.e., audition. Although there is evidence that the majority of odors are initially perceived as unpleasant, when retrieved from memory, pleasant connotations seem to dominate. The possible mechanisms for this dissociation are discussed.

Taste, smell and neuropsychological performance of individuals at familial risk for Alzheimer's disease.
Schiffman SS, Graham BG, Sattely-Miller EA, Zervakis J, Welsh-Bohmer K.
Department of Psychiatry, Duke University Medical Center, Durham, NC 27710, USA. sss@duke.edu

The purpose of the study was to determine whether there are chemosensory and neuropsychological changes that predate the onset of Alzheimer's disease in individuals at familial risk.
enhanced risk of developing the condition. To study this question, a unique sample of individuals (n = 33) was studied who were genetically at-risk for AD by virtue of documented multigenerational evidence of the disease (so-called multiplex families). The performance of at-risk individuals was evaluated on various smell, taste, and neuropsychological measures at baseline and 18 months later. Their performance was compared to a control group (n = 32) that was matched in age, gender, education, and race. At baseline the at-risk group performed worse than the control group on the chemosensory measures of phenethyl alcohol smell detection, smell memory, and taste memory, and on a memory measure involving recall of narrative information (Logical Memory I from the Wechsler Memory Scale- Revised). Across both sessions, the at-risk group had lower smell memory scores than the control group. At-risk status was not significantly associated with APOE status. The results of this and other studies suggest that individuals who are genetically at risk for developing AD may perform more poorly on memory and smell measures compared to those not at risk. This effect may be separate from one known genetic risk factor of AD, APOE, and supports that multiple genes are likely responsible for the disease and its associated memory and other neurocognitive symptoms.


Functional MRI of congenital hyposmia: brain activation to odors and imagination of odors and tastes.
Henkin RI, Levy LM.
Taste and Smell Clinic, Washington, DC 20016, USA. doc@tasteandsmell.com
PURPOSE: Our goal was to use functional MRI (fMRI) to define brain activation in response to odors and imagination ("memory") of odors and tastes in patients who never recognized odors (congenital hyposmia). METHOD: Functional MR brain scans were obtained in nine patients with congenital hyposmia using multislice echo planar imaging (EPI) in response to odors of amyl acetate, menthone, and pyridine and to imagination ("memory") of banana and peppermint odors and to salt and sweet tastes. Functional MR brain scans were compared with those in normal subjects and patients with acquired hyposmia. Activation images were derived using correlation analysis, and ratios of areas of brain activated to total and hemispheric brain areas were calculated. Total and hemispheric activated pixel counts were used to quantitate regional brain activation. RESULTS: Brain activation in response to odors was present in patients with congenital hyposmia. Activation was significantly lower than in normal subjects and patients with acquired hyposmia and did not demonstrate differential vapor pressure-dependent detection responsiveness or odor response lateralization. Regional activation localization was in anterior frontal and temporal cortex similar to that in normal subjects and patients with acquired hyposmia. Activation in response to presented odors was diverse, with a larger group exhibiting little or no activation with localization only in anterior frontal and temporal cortex and a smaller group exhibiting greater activation with localization extending to more complex olfactory integration sites. "Memory" of odors and tastes elicited activation in the same central nervous system (CNS) regions in which activation in response to presented odors occurred, but responses were significantly lower than in normal subjects and patients with acquired hyposmia and did not lateralize. CONCLUSION: Odors induced CNS activation in patients with congenital hyposmia, which distinguishes olfaction from vision and audition since neither light nor acoustic stimuli induce CNS activation. Odor activation localized to anterior frontal and temporal cortex, consistent with the hypothesis that olfactory pathways are hard-wired into the CNS and that
Further pathways are undeveloped with primary olfactory system CNS connections but lack of secondary connections. However, some patients exhibited greater odor activation with response localization extending to cingulate and opercular cortex, indicating some olfactory signals impinge on and maintain secondary connections consistent with similar functions in vision and audition. Activation localization of taste "memory" to anterior frontal and temporal cortex is consistent with CNS plasticity and cross-modal CNS reorganization as described for vision and audition. Thus, there are differences and similarities between olfaction, vision, and audition, the differences dependent on unique qualities of olfaction, perhaps due to its diffuse, primitive, fundamental role in survival. Response heterogeneity to odors may reflect heterogeneous genetic abnormalities, independent of anatomic or hormonal changes but dependent on molecular abnormalities in growth factor function interfering with growth factor/stem cell interactions. Patients with congenital hyposmia offer an unique model system not previously explored in which congenital smell lack as measured by fMRI is reflective of congenital dysfunction of a major sensory system.

**Olfactory functioning and cognitive abilities: a twin study.**
Finkel D, Pedersen NL, Larsson M.
School of Social Sciences, Indiana University Southeast, New Albany, 47150, USA.
dfinkel@ius.edu

A Swedish version of the National Geographic Smell Survey (Wysocki and Gilbert 1989) was completed by 227 twin pairs from the Swedish Adoption/Twin Study of Aging. Twins ranged in age from 45 to 89 years. Quantitative genetic analysis of four measures of olfactory functioning indicated moderate heritability for odor identification and perceived intensity and nonsignificant heritability for odor detection and perceived pleasantness. Bivariate analyses revealed that the relationship between odor identification and measures of verbal ability was primarily genetically mediated. The results provided further support for the hypothesis that odor identification and verbal ability in general tap the same cognitive domain.

Mem Cognit 2000 Sep;28(6):957-64
**Verbal coding in olfactory versus nonolfactory cognition.**
Herz RS.
Department of Psychology, Brown University, Providence, RI 02912, USA.
rachel_herz@brown.edu

Two paired-associate memory experiments were conducted to investigate verbal coding in olfactory versus nonolfactory cognition. Experiment 1 examined the effects of switching/not switching odors and visual items to words between encoding and test sessions. Experiment 2 examined switching/not switching perceptual odors and verbal-imagine versions of odors with each other. Experiment 1 showed that memory was impaired for odors but not visual cues when they were switched to their verbal form at test. Experiment 2 revealed that memory was impaired for both odors and verbal-imagine cues when they were switched in format at test and that odor sensory imagery was not accessed by the instruction to imagine a smell. Together, these findings
suggest that olfaction is distinguished from other sensory systems by the degree of verbal coding involved in associated cognitive processing.

J Neurophysiol 2000 Sep;84(3):1656-66

**Functional mapping of human brain in olfactory processing: a PET study.**
Department of Nuclear Medicine and Radiology, Institute of Development, Aging and Cancer, Tohoku University, Sendai 980-8575, Japan. ahmad@idac.tohoku.ac.jp

This study describes the functional anatomy of olfactory and visual naming and matching in humans, using positron emission tomography (PET). One baseline control task without olfactory or visual stimulation, one control task with simple olfactory and visual stimulation without cognition, one set of olfactory and visual naming tasks, and one set of olfactory and visual matching tasks were administered to eight normal volunteers. In the olfactory naming task (ON), odors from familiar items, associated with some verbal label, were to be named. Hence, it required long-term olfactory memory retrieval for stimulus recognition. The olfactory matching task (OM) involved differentiating a recently encoded unfamiliar odor from a sequentially presented group of unfamiliar odors. This required short-term olfactory memory retrieval for stimulus differentiation. The simple olfactory and visual stimulation resulted in activation of the left orbitofrontal region, the right piriform cortex, and the bilateral occipital cortex. During olfactory naming, activation was detected in the left cuneus, the right anterior cingulate gyrus, the left insula, and the cerebellum bilaterally. It appears that the effort to identify the origin of an odor involved semantic analysis and some degree of mental imagery. During olfactory matching, activation was observed in the left cuneus and the cerebellum bilaterally. This identified the brain areas activated during differentiation of one unlabeled odor from the others. In cross-task analysis, the region found to be specific for olfactory naming was the left cuneus. Our results show definite recruitment of the visual cortex in ON and OM tasks, most likely related to imagery component of these tasks. The cerebellar role in cognitive tasks has been recognized, but this is the first PET study that suggests that the human cerebellum may have a role in cognitive olfactory processing as well.

Mov Disord 2003 Apr;18(4):364-72

**Olfaction in neurodegenerative disorder.**
Hawkes C.
Essex Centre for Neuroscience, Oldchurch Hospital, Romford, Essex, United Kingdom.

There has been an increase of interest in olfactory dysfunction since it was realised that anosmia was a common feature of idiopathic Parkinson's disease (PD) and Alzheimer-type dementia (AD). It is an intriguing possibility that the first sign of a disorder hitherto regarded as one of movement or cognition may be that of disturbed smell sense. In this review of PD, parkinsonian syndromes, essential tremor, AD, motor neurone disease (MND) and Huntington's chorea (HC) the **following observations are made:** 1) olfactory dysfunction is frequent and
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Modulation of visual event-related potentials by emotional olfactory stimuli.
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The objective of the present study was to determine whether an olfactory prime could modulate behavior and visual event-related potentials (ERPs) obtained in response to a visual stimulation representing female faces. More specifically, we tested the hypothesis that a pleasant odor could have effects on face perception: behavioral effects on subjective emotional estimation of faces, and on associated response times, and electrophysiological effects on the N400 and late positive complex or LPC. Experiments were performed in which subjects had to decide whether the presented face was pleasant or not, while visual ERPs were recorded. Faces were always primed with either a pleasant odor or a neutral olfactory stimulus (pure air). In order to test the effect of subject's awareness, participants were not informed that an odor would be presented in the experimental sessions. Responses were significantly shorter for unpleasant faces. However, no behavioral effects of the pleasant odor on response time or on evaluation of face pleasantness were observed. Late ERPs evoked by faces were modulated by the presence of a pleasant odor, even when subjects were neither warned nor aware of the presence of the odor: in a frontal site and after the diffusion of the odor, the LPC (appearing 550 ms after the presentation of the visual stimulus) evoked by unpleasant faces was significantly more positive than the LPC evoked by pleasant faces. This effect could reflect an enhanced alert reaction to unpleasant faces are preceded by an (incongruous) pleasant odor.

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Autonomic nervous system responses to odours: the role of pleasantness and arousal.
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Olfactory identification and apolipoprotein E epsilon 4 allele in mild cognitive impairment.
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The amygdala and reward.
Baxter MG, Murray EA.
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The amygdala -- an almond-shaped group of nuclei at the heart of the telencephalon -- has been associated with a range of cognitive functions, including emotion, learning, memory, attention and perception. Most current views of amygdala function emphasize its role in negative emotions, such as fear, and in linking negative emotions with other aspects of cognition, such as learning and memory. However, recent evidence supports a role for the amygdala in processing positive emotions as well as negative ones, including learning about the beneficial biological value of stimuli. Indeed, the amygdala's role in stimulus-reward learning might be just as important as its role in processing negative affect and fear conditioning.

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2002, Vol. 24, No. 5, pp. 705±709
Brief Report:
Anosmia and Remote Outcome in Closed Head Injury
M. Frank Greiffenstein, W. John Baker, and Thomas Gola

The value of posttraumatic anosmia as a predictor of late social outcomes was examined in a sample of closed head injury (CHI) patients. Unemployment rates were equally high in both the anomic and nonanosmic closed head injury patients. The groups also did not differ in psychiatric or neuropsychological status. Anosmic patients had longer initial hospital stays and deeper initial comatose/confusional states. Anosmia does not appear to add incrementally to disability status and it does not automatically imply the presence of basal-frontal damage.

More with Affect.....

J Clin Psychiatry 2003 Feb;64(2):202-7
Olfaction as a traumatic reminder in posttraumatic stress disorder: case reports and review.
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BACKGROUND: Memory for odors that are associated with intense emotional experiences is often strongly engraved. Odors are claimed to be more closely connected to affect than other sensory experiences. They can serve as potent contextual cues for memory formation and emotional conditioning and can also serve as cues for olfactory flashbacks. Though trauma-related smells have long been noted by clinicians to be precipitants of traumatic memories in patients with posttraumatic stress disorder (PTSD), very few reports have been published that document this. CASE REPORTS: We review olfactory memories and olfactory flashbacks by presenting 3 cases that illustrate the role of olfaction in PTSD. In these cases olfaction is either a precipitant of PTSD symptoms or an important component of reexperiencing. DISCUSSION: In PTSD, seemingly nonspecific cues have the potential to precipitate traumatic memories with strong emotional components. These conditioned responses in PTSD are hypothesized to be mediated by specific brain areas, i.e., amygdala, hippocampus, and orbitofrontal cortex. Questions about smells as a traumatic reminder should be part of the routine assessment of intrusive memories in PTSD. In addition, smells may have the potential to provide cues to exposure situations in therapy or to facilitate de novo conditioning.

Affective experience has been described in terms of two primary dimensions: intensity and valence. In the human brain, it is intrinsically difficult to dissociate the neural coding of these affective dimensions for visual and auditory stimuli, but such dissociation is more readily achieved in olfaction, where intensity and valence can be manipulated independently. Using event-related functional magnetic resonance imaging (fMRI), we found amygdala activation to be associated with intensity, and not valence, of odors. Activity in regions of orbitofrontal cortex, in contrast, were associated with valence independent of intensity. These findings show that distinct olfactory regions subserve the analysis of the degree and quality of olfactory stimulation, suggesting that the affective representations of intensity and valence draw upon dissociable neural substrates.

A relationship between smell identification and empathy.
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Olfaction is a sense that has close relationships with the limbic system and emotion. Empathy is a vicarious feeling of others' emotional states. The two functions are known to be subserved by common neuroanatomical structures, including orbitofrontal cortex, mediodorsal
This study demonstrates a correlation between smell identification and empathy, using the Mehrabian and Epstein Empathy Questionnaire and Alberta Smell Test. Right nostril smell identification correlated with empathy, whereas the left nostril did not. Given the predominantly ipsilateral representation in the olfactory system, this is in accordance with right hemisphere dominance for emotional functions and empathy. Further, the emotional component of empathy (feeling another's emotions) correlated with smell, whereas a cognitive component (comprehending another's emotions) did not. This study is the first to demonstrate a relationship between empathy and smell in normal subjects, suggesting common neural substrates.

Distinct neuropsychological characteristics in Creutzfeldt-Jakob disease
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Objectives: To characterise the nature of cognitive change in Creutzfeldt-Jakob disease (CJD).
Methods: Case histories are reported of four patients with sporadic (sCJD) and two with familial CJD (fCJD), with postmortem pathological findings in four cases. The data derived from cognitive examination are examined with respect to the presence or absence of a variety of characteristics to elicit performance profiles across cognitive domains.
Results: Three patients with sCJD exhibited clear focal cortical deficits. One patient had visual impairment leading to cortical blindness, associated with posterior hemisphere abnormalities on single photon emission computed tomography (SPECT) imaging; two others had impairments in language, mirrored by left hemisphere SPECT abnormalities. The remaining three patients showed no specific cortical symptomatology. Despite these differences all six patients shared common qualitative characteristics: episodic unresponsiveness, interference effects, and profound verbal and motor perseveration. These common features are interpreted in terms of impaired activation and regulation of neocortex from subcortical structures. Findings from postmortem pathological examination and from the published literature provide converging evidence to implicate a critical role of the thalamus. Conclusion: These preliminary findings suggest that sCJD and fCJD may be associated with distinct neuropsychological characteristics.
Chronic fatigue syndrome following a toxic exposure. Racciatti D, Vecchiet J, Ceccomancini A, Ricci F, Pizzigallo E. Department of Infectious Diseases, G. D'Annunzio University, Chieti Scalo, Italy.

racciatt@unich.it Chronic fatigue syndrome (CFS) is a clinical entity characterized by severe fatigue lasting more than 6 months and other well-defined symptoms. Even though in most CFS cases the etiology is still unknown, sometimes the mode of presentation of the illness implicates the exposure to chemical and/or food toxins as precipitating factors: ciguatera poisoning, sick building syndrome, Gulf War syndrome, exposure to organochlorine pesticides, etc. In the National Reference Center for CFS Study at the Department of Infectious Diseases of 'G. D'Annunzio' University (Chieti) we examined five patients (three females and two males, mean age: 37.5 years) who developed the clinical features of CFS several months after the exposure to environmental toxic factors: ciguatera poisoning in two cases, and exposure to solvents in the other three cases. These patients were compared and contrasted with two sex- and age-matched subgroups of CFS patients without any history of exposure to toxins: the first subgroup consisted of patients with CFS onset following an EBV infection (post-infectious CFS), and the second of patients with a concurrent diagnosis of major depression. All subjects were investigated by clinical examination, neurophysiological and immunologic studies, and neuroendocrine tests. Patients exposed to toxic factors had disturbances of hypothalamic function similar to those in controls and, above all, showed more severe dysfunction of the immune system with an abnormal CD4/CD8 ratio, and in three of such cases with decreased levels of NK cells (CD56+). These findings may help in understanding the pathogenetic mechanisms involved in CFS.

Pre-sleep imagery under the microscope: a comparison of patients with insomnia and good sleepers

Behaviour Research and Therapy Volume 41, Issue 3 March 2003 Pages 273-284
J. Nelson and A. G. Harvey

During the pre-sleep period and in the natural home environment patients with insomnia (N=20) and good sleepers (N=20) were asked to record when an image came to mind by pressing a handheld counter. They then provided an oral description of the image and indicated whether the image was 'pleasant', 'unpleasant', or 'neutral' (responses captured via a voice-activated tape recorder). Subjective and objective (actigraphy) estimates of sleep-onset latency (SOL) were recorded. On both the handheld counter and the audiotape recording, participants with insomnia reported fewer images than the good sleepers. The insomnia group had a higher percentage of unpleasant images compared to good sleepers. For the insomnia group, but not the good sleeper...
group, there was a positive correlation between unpleasant images and subjective SOL. The insomnia group experienced more images regarding 'intimate relationships' and 'sleep' and fewer regarding 'random/non-connected topics' compared to the good sleeper group. The results are discussed with reference to proposals made by Borkovec, Ray and Stöber (Cognitive Ther. Res., 22, (1998) 561) in the context of generalised anxiety disorder (GAD).

Motherhood as a vulnerability factor in major depression: the role of negative pregnancy experiences
Social Science & Medicine Volume 56, Issue 6 March 2003 Pages 1249-1260
Odette Bernazzani, , a and Antonia Bifulcob

Adverse pregnancy experiences were examined retrospectively in relation to adult lifetime experience of clinical depression to see whether such experience conferred long-term risk for women. The sample consisted of just under 200 community-based women, half of whom were selected for high depressive-risk on the basis of adverse childhood experience. Over two-thirds of these women had experienced pregnancy. Adverse pregnancies were classified either in terms of loss (adverse non-live pregnancy/births) or in terms of live births in difficult circumstances (adverse live pregnancy/births). Intensive life history interviews collected details of all pregnancies, childhood neglect/abuse, marital adversity and a history of episodes of clinical depression.

Both adverse non-live and live pregnancy experiences were significantly related to lifetime depression. The relationship remained for depression in different time periods and for those episodes unrelated to maternity experience. Both types of adverse pregnancy/birth experiences were associated with increased rates of marital problems. While adverse live pregnancy/births related to prior childhood neglect/abuse, this did not hold for those non-live. Logistic regression showed that only adverse non-live pregnancy/births together with marital adversity and childhood neglect/abuse provided the best model for lifetime depression. The findings are discussed in terms of lifetime trajectories linking difficult environments, close relationships and issues of loss.

Sociological influences on antidepressant prescribing
Social Science & Medicine Volume 56, Issue 6 March 2003 Pages 1335-1344
Betsy Sleath, , a and Ya-Chen Tina Shiha, b

This study examined how patient characteristics, physician characteristics, the physician's interaction with the health care system, and the physician's interaction with the patient influenced whether patients with a depression diagnosis received an antidepressant prescription and whether they received a SSRI antidepressant, a non-SSRI antidepressant, or both. The 1998 National Ambulatory Medical Care Survey (NAMCS), in the USA, was used for the analysis. Logistic regression was used to examine what characteristics influenced whether a patient with a depression diagnosis received an antidepressant prescription. Next, a multinomial
logistic regression model was applied to examine the relative risk of using one type of antidepressant versus another among antidepressant users while correcting for possible sample selections using the Heckman selection model. Sixty-seven percent of patients with a depression diagnosis received an antidepressant. Patients who were seeing providers who were not primary care physicians or psychiatrists, self-paying patients, and patients with neurotic depression were significantly less likely to receive an antidepressant prescription. Patients with depression listed as their first diagnosis were significantly more likely to receive an antidepressant prescription. Patients seeing a psychiatrist were more likely than patients seeing a primary care physician to receive a non-SSRI antidepressant than a SSRI antidepressant. Patients belonging to an HMO that had capitated visits were over four times more likely to receive non-SSRI antidepressants than SSRI antidepressants. Patients with major depression were significantly more likely to receive a non-SSRI antidepressant. Patients with depression as their primary diagnosis and patients who saw psychiatrists were significantly more likely to receive both SSRI and non-SSRI antidepressants rather than just SSRI antidepressants. Patient characteristics, physician characteristics, the physician's interaction with the health care system, and the physician's interaction with the patient all influenced antidepressant prescribing. An especially important finding was that insurance status influenced whether patients received an antidepressant. Health care providers need to take the time to help patients without insurance obtain antidepressant medication if it is needed.

Curr Neurol Neurosci Rep 2003 Mar;3(2):97-103

Fibromyalgia, fatigue, and headache disorders.
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Fibromyalgia, chronic fatigue, and primary headaches are common and debilitating disorders, and their related symptoms of widespread pain, fatigue, and headache have complex interactions and different implications for classification, diagnosis, mechanisms, and treatment. The "continuum" or "spectrum" idea and the modular headache theory are fundamental concepts in understanding these interactions. The overlap between symptom-based conditions leads the reasons to consider them as "functional somatic syndromes." Management of these patients includes a correct diagnosis, appropriate investigation for associated conditions, adequate treatment, and considering the therapeutic opportunities and limitations the comorbid disorders may impose.

Depress Anxiety 2003;17(1):34-42

Childhood adversities associated with major depression and/or anxiety disorders in a community sample of Ontario: Issues of co-morbidity and specificity.
Levitan RD, Rector NA, Sheldon T, Goering P.
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It has been well established that early adversity is a major risk factor for depression and for anxiety disorders in various populations and age groups. Few studies have considered the
relative strength of these associations and the possible role of co-morbid depression/anxiety in understanding them. Using data from a large community sample of Ontario, Canada, we examined the relative strength of the associations between early physical abuse, sexual abuse, and/or parental strain with depression alone, anxiety alone, and co-morbid depression/anxiety. The current sample consisted of 6,597 individuals 15-64 years of age who were interviewed using the World Health Organization Composite International Diagnostic Interview (CIDI). Using a multivariate design, we compared early adversity scores across four diagnostic study groups including normal controls, individuals with major depression but no anxiety disorders, individuals with one or more anxiety disorders without major depression, and individuals with co-morbid major depression and anxiety. Individuals with past disorders were considered separately from those with current disorders. For both past and current disorders, highly significant differences in early adversity scores were found across the four study groups. A novel and robust finding, consistent across all analyses, was a marked association between early sexual abuse and co-morbid depression and anxiety but not the "pure" disorders. A strong association between early parental strain and major depression (independent of anxiety) was also found. The overall pattern of results suggest that there may be unique relationships linking particular adversities to particular manifestations of depression and anxiety disorders later in life. A particularly strong association between early sexual abuse and co-morbid depression/anxiety was found.

Arch Women Ment Health 2003 Feb;6(1):15-22
Neurobiological effects of childhood abuse: implications for the pathophysiology of depression and anxiety.
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Mood and anxiety disorders are highly prevalent psychiatric disorders, especially in women, and they are associated with significant morbidity and mortality. A considerable literature indicates that vulnerability to depression and anxiety disorders is markedly increased by childhood abuse, e.g., physical, sexual, and psychological abuse, as well as adulthood stressors, e.g., death of a spouse. Little is known about the developmental neurobiological mechanisms by which childhood abuse increases the susceptibility of women to the development of depression and anxiety disorders in adulthood. Recent research on the effects of adverse early life experiences on central nervous system (CNS) stress systems has provided a greater understanding of the link between childhood abuse and susceptibility to mood and anxiety disorders. Specifically, early life traumatic events, occurring during a period of neuronal plasticity, appear to permanently render neuroendocrine stress response systems supersensitive. These physiological maladaptations likely represent long-term risk factors for the development of psychopathology after exposure to additional stress.

Dopamine genes and attention-deficit hyperactivity disorder: a review.
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OBJECTIVE: To review the results of genetic studies investigating dopamine-related genes in attention-deficit hyperactivity disorder (ADHD). DATA SOURCES: Papers (association/linkage, meta-analyses and animal model studies) were identified through searches of the PubMed database and systematically reviewed. DATA SYNTHESIS: Consistent results from molecular genetic studies are pointing strongly to the possible link between 2 specific genes, the dopamine transporter (SLC3A6) and the dopamine receptor 4 (DRD4), and ADHD. CONCLUSIONS: The implication of SLC6A3 and DRD4 genes in ADHD appears to be one of the most replicated in psychiatric genetics and strongly suggests the involvement of the brain dopamine systems in the pathogenesis of ADHD. However, more work is required to further these findings by genotype-to-phenotype correlations and identify the functional allelic variants/mutations that are responsible for these associations. The role of other dopamine genes, which may have smaller effects than SLC6A3 and DRD4, needs also to be determined.

Psychiatry Res 2003 Jan 20;122(1):13-9

A preliminary morphometric magnetic resonance imaging study of regional brain volumes in body dysmorphic disorder.


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Morphometric magnetic resonance imaging (MRI) was used to compare regional brain volumes in eight women with body dysmorphic disorder (BDD) and eight healthy comparison subjects. The BDD group exhibited a relative leftward shift in caudate asymmetry and greater total white matter vs. the comparison group. Findings with respect to the caudate nucleus are consistent with both the conceptualization of BDD as an obsessive-compulsive spectrum disorder, and the 'striatal topography model' of obsessive-compulsive disorders.

Clin Sci (Lond) 2003 Feb 18; [epub ahead of print]

Blood flow and muscle metabolism in chronic fatigue syndrome.

McCully KK, Smith S, Rajaei S, Leigh Jr JS, Natelson BH.

The purpose of this study was to determine if chronic fatigue syndrome (CFS) is associated with reduced blood flow and oxidative delivery to skeletal muscle. Patients with CFS according to CDC criteria (n=19) were compared to normal sedentary subjects (n = 11). Muscle blood flow was measured with Doppler ultrasound after cuff ischemia and after exercise. Muscle oxygen delivery was measured as the rate of post-exercise and post-ischemic oxygen-heme resaturation. Oxygen-heme resaturation was measured in the medial gastrocnemius muscle using continuous wavelength near-infrared spectroscopy. Muscle metabolism was measured using 31P magnetic resonance spectroscopy. CFS and controls were not different in the peak blood flow...
after cuff ischemia, the rate of recovery of phosphocreatine after submaximal exercise, and the rate of recovery of oxygen saturation after cuff ischemia. **In conclusion, CFS patients showed no deficit in blood flow or oxidative metabolism. This suggests that CFS symptoms do not require abnormal peripheral function.**

Neuropsychopharmacology 2003 Feb;28(2):348-58

**State Markers of Depression in Sleep EEG: Dependency on Drug and Gender in Patients Treated with Tianeptine or Paroxetine.**

Murck H, Nickel T, Kunzel H, Antonijevic IA, Schill J, Zobel A, Steiger A, Sonntag A, Holsboer F.

Tianeptine enhances while paroxetine inhibits serotonin reuptake into neurons; however, both show an antidepressive action. A subgroup of 38 depressed patients from a drug trial comparing the efficacy of tianeptine with that of paroxetine was studied with regard to their effects on sleep regulation, especially in relation to treatment response. We recorded sleep EEGs at day 7 and day 42 after the start of treatment with either compound, which allows measurement of changes due to the antidepressive medication in relation to the duration of treatment. Spectral analysis of the non-REM sleep EEG revealed a strong decline in the higher sigma frequency range (14-16 Hz) in male treatment responders independent of medication, whereas nonresponders did not show marked changes in this frequency range independent of gender. The patients receiving paroxetine showed less REM sleep and more intermittent wakefulness compared to the patients receiving tianeptine. REM density after 1 week of treatment was a predictor of treatment response in the whole sample. Psychopathological features with regard to the score in single items of the HAMD revealed predictive markers for response, some of which were opposite in the gender groups, especially those related to somatic anxiety. Changes in REM density were inversely correlated to the changes in HAMD in the paroxetine, but not the tianeptine, group. Our data suggest the importance of taking gender into account in the study of the biological effects of drugs. The study further points to the importance of the higher sigma frequency range in the sleep EEG of non-REM sleep and REM density as a marker of treatment response.

World J Biol Psychiatry 2001 Apr;2(2):83-8

**Structural neuroimaging studies in late-life depression: a review.**

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Which patients presenting with depression in late life will progress to a dementia syndrome has been an important research question in recent times. In this paper we review selectively structural neuroimaging investigations of late-life depression (LLD) that have been performed over the past two decades. These studies indicate that there are neuroimaging changes...
commonly observed in LLD patients when compared to normal controls. Findings include ventricular enlargement and sulcal widening, and reduction in volume size of frontal lobes, hippocampus and caudate nucleus. White matter lesions are more common in depressed subjects and tend to be more severe. Some studies report these changes to be more pronounced in patients who present with late-onset depression (LOD) but this has been contradicted by other studies. Preliminary work suggests that these changes may be associated with a poor prognosis but there is a dearth of systematic, well-controlled longitudinal studies.

Sleep in posttraumatic stress disorder.
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Posttraumatic stress disorder (PTSD) is often associated with sleep disturbances. In this review, we focus on the published literature on subjective and objective findings of sleep in patients with PTSD. Insomnia and nightmares are most commonly reported subjective sleep disturbances. Polysomnographic investigations have frequently reported rapid eye movement (REM) sleep abnormalities in PTSD. However, studies have not been consistent about the type of REM sleep dysfunction in PTSD patients. Antidepressants such as nefazodone, trazodone, fluvoxamine, and imagery rehearsal therapy are found to be beneficial in the treatment of PTSD associated sleep disturbances as well as core symptoms of this anxiety disorder. We propose use of such modalities of treatment in PTSD patients with predominant sleep disturbances. Further studies are required to clarify polysomnographic sleep changes especially role of REM sleep dysregulation and treatment of sleep disturbances in PTSD.

Trends Neurosci 2003 Mar;26(3):123-4
When neurons form memories.
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Although long-term memory is central among our cognitive functions, the search for a direct neurophysiological correlate to it has proven difficult. The formation of new memories depends on the hippocampus and adjacent cortex, but the final storage is thought to be in a widely distributed neocortical network. Recent experiments, using simultaneous recordings from hundreds of sites in monkey neocortex, have revealed the activation of such a distributed network - probably reflecting the consolidation of long-term memory storage.
Bursts as a unit of neural information: selective communication via resonance.
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What is the functional significance of generating a burst of spikes, as opposed to a single spike? A dominant point of view is that bursts are needed to increase the reliability of communication between neurons. Here, we discuss the alternative, but complementary, hypothesis: bursts with specific resonant interspike frequencies are more likely to cause a postsynaptic cell to fire than are bursts with higher or lower frequencies. Such a frequency preference might occur at the level of individual synapses because of the interplay between short-term synaptic depression and facilitation, or at the postsynaptic cell level because of subthreshold membrane potential oscillations and resonance. As a result, the same burst could resonate for some synapses or cells and not resonate for others, depending on their natural resonance frequencies. This observation suggests that, in addition to increasing reliability of synaptic transmission, bursts of action potentials might provide effective mechanisms for selective communication between neurons.

Substance use and cognition in early psychosis.
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OBJECTIVE: To determine the relation between substance use and cognition in individuals experiencing their first episode of psychosis. DESIGN: Prospective cross-sectional and longitudinal study. SETTING: An Early Psychosis Treatment and Prevention Program, an outpatient clinic in a psychiatry department at a university-affiliated hospital. PARTICIPANTS: Individuals with a psychotic illness who were admitted to an Early Psychosis Program; 266 patients were assessed at initial presentation, 159 at 1 year and 90 at 2 years. Most were outpatients. MEASURES: The effects of substance use (alcohol, cannabis, hallucinogens, cocaine, stimulants) on cognition were assessed. Substance use was determined by DSM-IV criteria, and the Case Manager Rating Scale was used to determine the level of substance use. A comprehensive cognitive battery of tests was used, and the Positive and Negative Syndrome Scale for schizophrenia was administered to all subjects to determine levels of positive and negative symptoms. RESULTS: Overall, both cross-sectionally and longitudinally, there were no significant associations between cognitive functioning and the use of various substances. Substance use was associated with higher positive symptoms. CONCLUSIONS: Individuals with psychotic disorders who show mild-to-moderate abuse of substances, in particular alcohol and cannabis, do not exhibit more cognitive impairment than those who do not do use the substances. However, substance use may have other detrimental effects on the process of the psychotic illness.

A large body of evidence indicates that people attribute unwarranted causality (influence) to a stimulus simply because it is more noticeable or salient than other available stimuli. This article reviews recent research demonstrating that this illusory-causation phenomenon can
produce serious prejudicial effects with regard to how people evaluate certain types of evidence. Specifically, evaluations of videotaped confessions can be significantly altered by presumably inconsequential changes in the camera perspective taken when the confessions are initially recorded. Videotaped confessions recorded with the camera focused on the suspect -- compared with videotapes from other camera points of view (e.g., focused equally on the suspect and interrogator) or with more traditional presentation formats (i.e., transcripts and audiotapes) -- lead mock jurors to judge that the confessions were more voluntary and, most important, that the suspects are more likely to be guilty. Because actual criminal interrogations are customarily videotaped with the camera lens zeroed in on the suspect, these findings are of considerable practical significance.

Neuroreport 2002 Jan 21;13(1):29-33
A randomised, placebo-controlled, double blind study of treatment of Huntington's disease with unsaturated fatty acids.
Vaddadi KS, Soosai E, Chiu E, Dingjan P.
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Huntington's Disease (HD) is a serious dominantly inherited neurodegenerative disorder for which there are no current treatments. Open label and animal studies have suggested that highly unsaturated fatty acids (HUFA) may be beneficial. Seventeen patients with HD were entered into a randomised, placebo-controlled, double blind trial of HUFA therapy. Patients were assessed on the Rockland-Simpson Dyskinesia Rating Scale (RSDRS) and the Unified Huntington's Disease Rating Scale (UHDRS). On the RSDRS and the UHDRS motor scale patients on HUFA treatment improved while those on placebo deteriorated, with a significant difference between the two groups on the RSDRS. A similar trend was noted on the UHDRS functional performance scales. Little change was seen on the neuropsychology scales. There were no treatment-related adverse events. This is the first time that a significant improvement has been noted in a randomised trial in HD. The results are consistent with open label observations; a second placebo-controlled study in end-stage patients, and a study in a transgenic mouse model of HD.

Gable L, Shklar B, Gave D

Background: Stimulation of the antinociceptive system by electrical current from electrodes placed on the head is a renewed method of pain relief. Methods: We conducted a randomized, double blind placebo controlled study on 20 chronic back pain patient. They were treated with either transcranial electrostimulation (TCES) or an active placebo device. Pain level and serum /3-endorphin levels were measured before and after treatment. Results: /3-Endorphin level increased in seven of ten patients from the treatment group and did not change in control group (P = 0.057 between groups) Pain level decreased in eight treated patients and seven control patients (significant decrease for each group, no significant difference between groups). Conclusions: Transcranial electrostimulation is a nonpharmacologic method of pain relief accompanied or mediated by /3-endorphin release. The comparable degree of the initial clinical response
emphasizes the powerful placebo effect on reported pain not mediated by endorphin release. This preliminary study shows that noninvasive electrical stimulation is a safe treatment with a positive effect on \( \beta \)-endorphin blood levels.

Psychological Medicine (2003), 33:197-201

Editorial

**Costs, correlates and consequences of fatigue in children and adults**

PETER D. WHITE c1

**Abstract**

The problems of understanding what causes chronic fatigue, its relationship to psychiatric disorders, and how best to treat it continue to baffle and bemuse clinicians and patients alike (Report to the CMO, 2002; Stanley et al. 2002). This edition of the journal carries four original papers that provide much needed knowledge in a subject riddled by polemic and prejudice.

Psychological Medicine (2003), 33:217-227

**Computerized, interactive, multimedia cognitive-behavioural program for anxiety and depression in general practice**

J. PROUDFOOT a1 c1, D. GOLDBERG a1, A. MANN a1, B. EVERITT a1, I. MARKS a1 and J. A. GRAY a1

**Background.** Cognitive-behavioural therapy (CBT) brings about significant clinical improvement in anxiety and depression, but therapists are in short supply. We report the first phase of a randomized controlled trial of an interactive multimedia program of cognitive-behavioural techniques, Beating the Blues™ (BtB), in the treatment of patients in general practice with anxiety, depression or mixed anxiety/depression.

**Method.** One hundred and sixty-seven adults suffering from anxiety and/or depression and not receiving any form of psychological treatment or counselling were randomly allocated to receive, with or without medication, BtB or treatment as usual (TAU). Measures were taken on five occasions: prior to treatment, 2 months later, and at 1, 3 and 6 months follow-up using the Beck Depression Inventory, Beck Anxiety Inventory and Work and Social Adjustment Scale.

**Results.** Patients who received BtB showed significantly greater improvement in depression and anxiety compared to TAU by the end of treatment (2 months) and to 6 months follow-up. Symptom reduction was paralleled by improvement in work and social adjustment. There were no interactions of BtB with concomitant pharmacotherapy or duration of illness, but evidence, on the Beck Anxiety Inventory only, of interaction with primary care practice. Importantly, there was no interaction between the effects of BtB and baseline severity of depression, from which we conclude that the effects of the computer program are independent of starting level of depression.

**Conclusions.** These results demonstrate that computerized interactive multimedia cognitive-behavioural techniques under minimal clinical supervision can bring about improvements in depression and anxiety, as well as in work and social adjustment, with and without pharmacotherapy and in patients with pre-treatment illness of durations greater or less than 6 months. Thus, our results indicate that wider dissemination of cognitive-behavioural techniques is possible for patients suffering from anxiety and/or depressio...
Learning disability and epilepsy in an epidemiological sample of individuals with tuberous sclerosis complex

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Background. Intellectual impairments are a recognized feature of tuberous sclerosis complex (TSC), but the frequency and degree of intellectual impairments has not been systematically studied in large epidemiological samples using standardized measures. As such, the form of the IQ distribution (uni- or bi-modal) has not been established and the relationship between IQ and other features (e.g. epilepsy history) is poorly delineated. To address these shortcomings, we assessed the intellectual abilities of a large epidemiological sample of individuals with TSC, drawn from the ‘Wessex’ area of SW England and compared them with the abilities of their unaffected siblings.

Method. Standardized tests were used to estimate the abilities of 108 (56 males, 52 females, median age=25, range=4–75) individuals with TSC and 29 unaffected siblings (14 males, 15 females, median age=18, range=6–55). Seizure history was obtained from informants and medical records.

Results. Estimated IQ was bi-modally distributed: 55·5% had an IQ in the normal range; 14% had mild to severe impairments; and 30·5% had profound disability (IQ<21). Forty-four per cent of the individuals with TSC had an IQ<70. In the subset of normally intelligent individuals with TSC, IQ was normally distributed with a mean of 93·6. This mean was significantly lower than the mean IQ of unaffected siblings (IQ=105·6). All individuals with learning disability had a history of seizures that usually commenced before 12 months of age and that often presented as infantile spasms. Multivariate analyses indicated that a history of seizures as well as a history of infantile spasms was predictive of the degree of intellectual impairment.

Conclusions. Intellectual abilities were bi-modally distributed in a representative sample of individuals with TSC. The likelihood of impairment was associated with a history of seizures, particularly infantile spasms. The genetic and brain basis of these findings requires further investigation.

Pattern of cognitive dysfunction in depressive patients during maintenance electroconvulsive therapy

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Psychological Medicine (2003), 33:345-350

Brief Communication

Pattern of cognitive dysfunction in depressive patients during maintenance electroconvulsive therapy
Background. Objective data regarding adverse cognitive deficits associated with maintenance electroconvulsive therapy (M-ECT) are lacking. This study examined the cognitive state of depressive patients during M-ECT.

Method. A cross-sectional study was carried out in 11 depressive patients in remission, all with a DSM-IV diagnosis of major depressive disorder. The mean number of previous ECT sessions was 36·1, and the mean intersession interval was 52·7 days. A group of 11 patients who had not received ECT was selected for comparison and matched for diagnosis, sex, age and years of schooling. All subjects were assessed using a complete neuropsychological battery including memory, attention and frontal function tests.

Results. Groups did not present differences in long delay verbal recall. Encoding of new information and results on the frontal function tests were significantly lower in the M-ECT patients.

Conclusion. Depressed patients preserve long-term memory, but suffer short-term memory impairment and frontal function alteration during M-ECT. Further longitudinal studies are necessary to determine the influence of M-ECT on non-memory functions and different memory subtypes.

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Psychological Medicine (2003), 33:41-49

Effects of acute tryptophan depletion on cognitive function in Alzheimer's disease and in the healthy elderly

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Background. The cholinergic system is profoundly impaired in senile dementia of Alzheimer type (SDAT) and replacement therapy produces only modest clinical benefits. The serotonergic system is also impaired and may contribute both to cognitive and non-cognitive symptoms in SDAT. To investigate this further we assessed the effects of lowering brain serotonin using the technique of acute tryptophan depletion on cognitive function in patients with SDAT and in age matched control subjects.

Method. Sixteen patients with probable SDAT and 17 healthy elderly subjects received two amino acid drinks in a within subject, double-blind, placebo-controlled, counterbalanced, crossover design. One of the drinks was nutritionally balanced and contained tryptophan (placebo), the other was identical but contained no tryptophan. A battery of detailed neuropsychological tests was performed between 4 and 6 h after the drink. Mood rating scales and other ratings of behavioural and emotional symptoms were also performed on both occasions.
Results. Acute tryptophan depletion resulted in impairment on tasks of working memory in both groups. There was no group specific effect. Female SDAT subjects performed better on a task of pattern recognition during acute tryptophan depletion compared with placebo. There were no changes in behavioural symptoms during acute tryptophan depletion in either group.

Conclusion. Compromised serotonergic function may be an important contributor to cognitive decline in SDAT and in ageing. Strategies targeting specific 5HT receptors may be helpful in SDAT.

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The use of neurofeedback as an operant conditioning paradigm has disclosed that participants are able to gain some control over particular aspects of their electroencephalogram (EEG). Based on the association between theta activity (4-7 Hz) and working memory performance, and sensorimotor rhythm (SMR) activity (12-15 Hz) and attentional processing, we investigated the possibility that training healthy individuals to enhance either of these frequencies would specifically influence a particular aspect of cognitive performance, relative to a non-neurofeedback control-group. The results revealed that after eight sessions of neurofeedback the SMR-group were able to selectively enhance their SMR activity, as indexed by increased SMR/theta and SMR/beta ratios. In contrast, those trained to selectively enhance theta activity failed to exhibit any changes in their EEG. Furthermore, the SMR-group exhibited a significant and clear improvement in cued recall performance, using a semantic working memory task, and to a lesser extent showed improved accuracy of focused attentional processing using a 2-sequence continuous performance task. This suggests that normal healthy individuals can learn to increase a specific component of their EEG activity, and that such enhanced activity may facilitate semantic processing in a working memory task and to a lesser extent focused attention. We discuss possible mechanisms that could mediate such effects and indicate a number of directions for future research.

CNS Drugs 2003;17(2):101-15
Related Articles, Links

Coordination in the dynamics of the brain as inferred from EEG analysis.
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The present study observed the coordination between cortical areas during no task conditions as well as for the pathological condition of epilepsy, by application of the phase synchronization technique to the EEG signal in a multichannel recording. The index obtained from the phase entrainment investigation was properly scaled by a novel method to take into account the effect of nearest neighbor interactions. This scaled index was analyzed temporally to learn about the behavior of regional interactions in time. The results obtained not only corroborate earlier known results, but also give deeper insight into actual brain functioning.


**Ritalin revisited: does it really help in neurological injury?**
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Methylphenidate (Ritalin) is a commonly used central nervous stimulant. It has been used in various neurological conditions, including attention deficit disorder, depression, and narcolepsy. Methylphenidate has been advocated in patients with traumatic brain injury and stroke for a variety of cognitive, attention, and behavioral problems. It also has been shown to speed recovery from poststroke depression so that patients can participate more fully in rehabilitation programs. Research suggests that it also may have a role in augmenting activity of injured neuronal tissue in the comatose patient, thus facilitating a return to consciousness. The neuroscience nurse plays an important role in monitoring response to Ritalin, including identifying its side effects. A review of the limited studies on the use of Ritalin, its mechanisms of action, dosing, and weaning provide a current understanding of this adjunctive agent's role in treatment for the neurological population.

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**Executive dysfunction following traumatic brain injury: Neural substrates and treatment strategies.**
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Executive dysfunction is among the most common and disabling aspects of cognitive impairment following traumatic brain injury (TBI), and may include deficits in reasoning, planning, concept formation, mental flexibility, aspects of attention and awareness, and purposeful behavior. These impairments are generally attributed to frontal systems dysfunction, due either to direct insult to the frontal lobes or to disruption of their connections to other brain regions. Evaluation of executive deficits typically includes neuropsychological assessment, though adjunctive interviews can be critical in detecting subtle dysexecutive symptoms that may not be apparent on standardized testing. Rehabilitation programs emphasizing cognitive-behavioral approaches to the retraining of planning and problem-solving skills can be effective in ameliorating identified executive deficits. In addition, pharmacological approaches may be
useful in addressing aspects of executive dysfunction. This review summarizes the nature of executive deficits following TBI, their neuroanatomical substrates, selected assessment and treatment strategies, and recent research findings and trends.

Peptides 2002 Dec;23(12):2307-65

**Endogenous opiates and behavior: 2001.**

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This paper is the twenty-fourth installment of the annual review of research concerning the opiate system. It summarizes papers published during 2001 that studied the behavioral effects of the opiate peptides and antagonists. The particular topics covered this year include the molecular-biochemical effects and neurochemical localization studies of endogenous opioids and their receptors (I), and the roles of these opioid peptides and receptors in pain and analgesia (); stress and social status (); tolerance and dependence (); learning and memory (); eating and drinking (); alcohol and drugs of abuse (); sexual activity and hormones, pregnancy, development and endocrinology (); mental illness and mood (); seizures and neurologic disorders (); electrical-related activity and neurophysiology (); general activity and locomotion (); gastrointestinal, renal and hepatic functions (); cardiovascular responses (); respiration and thermoregulation (); and immunological responses (I).

Psychophysiology (2002), 39:723-732

**Stress and selective attention: The interplay of mood, cortisol levels, and emotional information processing**

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The effects of a stressful challenge on the processing of emotional words were examined in college students. Stress induction was achieved using a competitive computer task, where the individual either repeatedly lost or won against a confederate. Mood, attention, and cortisol were recorded during the study. There were four findings: (1) Participants in the negative stressor condition were faster to shift attention away from negative words than positive or neutral words; (2) attentional shifts away from negative words were associated with stress-induced mood lowering; (3) participants in the negative stress condition with elevated scores on the Beck Depression Inventory were slow to disengage attention from all stimuli; and (4) elevated depression scores were associated with lower cortisol change from baseline during the experimental phase, and with higher cortisol levels during the recovery phase. These findings point to information-processing strategies as a means to regulate emotion, and to atypical
features of cognitive and adrenocortical function that may serve as putative risk markers of depression.

**Fitness Effects on the Cognitive Function of Older Adults: A Meta–Analytic Study**
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A meta–analytic study was conducted to examine the hypothesis that aerobic fitness training enhances the cognitive vitality of healthy but sedentary older adults. Eighteen intervention studies published between 1966 and 2001 were entered into the analysis. Several theoretically and practically important results were obtained. Most important, fitness training was found to have robust but selective benefits for cognition, with the largest fitness–induced benefits occurring for executive–control processes. The magnitude of fitness effects on cognition was also moderated by a number of programmatic and methodological factors, including the length of the fitness–training intervention, the type of the intervention, the duration of training sessions, and the gender of the study participants. The results are discussed in terms of recent neuroscientific and psychological data that indicate cognitive and neural plasticity is maintained throughout the life span.

**Models of Consistency**
Psychological Science, March 2003, vol. 14, no. 2, pp. 131-137(7)
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This article presents a theory of how individuals detect whether descriptions of an entity are consistent or inconsistent. The theory postulates that individuals try to construct a mental model of the entity in which all the propositions are true. If they succeed, they infer that the description is consistent; otherwise, they infer that it is inconsistent. We report three experiments that corroborated the theory. Experiment 1 confirmed that evaluating consistency is easier when an initial model suffices than when reasoners have to find an alternative model. Experiment 2 established the occurrence of illusory inferences about the properties of entities. Experiment 3 showed that the illusions correspond to mental models of the assertions, even when these models are wrong because they fail to represent what is false.

Psychoneuroendocrinology
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Impact of a unilateral brain lesion on cortisol secretion and emotional state: anterior/posterior dissociation in humans
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The main goal of this study was to evaluate whether a unilateral brain lesion in a human population is associated with a modification of the circadian cortisol secretion profile, and/or patient's emotional state. The second goal of this study was to assess whether there would be differences in both the pattern of cortisol secretion and emotional state in brain-damaged patients as a function of side of lesion, and localization (anterior vs posterior) of lesion. Eight patients with a left cortical lesion, six patients with a right cortical lesion, four patients with basal ganglia lesions (2 left and 2 right) and ten healthy volunteers were evaluated daily on measures of salivary cortisol levels and subjective feelings of joy and sadness at 0700, 1200, 1600 and 1900 hours over a 15-day period. Patients with cortical brain lesions presented higher cortisol levels and higher scores of sadness at the time of the morning peak (7:00 am), when compared to healthy volunteers and patients with basal ganglia lesions. Laterality of the lesion was not related to cortisol secretion, but frontal damage (anterior lesion) was associated with higher cortisol levels at the time of the morning peak (7:00 am) when compared to more posterior damage. There was no significant correlation between basal circulating levels of cortisol and emotional states in patients and healthy subjects. The results of this study suggest that hypothalamic–pituitary–adrenal (HPA) axis dysregulation is associated with unilateral injury particularly in frontal areas. These results, obtained in a human population, go along with recent animal studies reporting an implication of frontal regions in HPA activity.
neuropsychological testing and self report of dysexecutive function and post-concussion symptoms were acquired to characterise the sample.

Results: There was no difference between patients and controls in normalised regional cerebral FDG uptake in the resting state in frontal and temporal regions selected a priori. However, during the spatial working memory task, patients had a smaller increase in rCBF than controls in the right prefrontal cortex.

Conclusions: Persistent post-concussive symptoms may not be associated with resting state hypometabolism. A cognitive challenge may be necessary to detect cerebral changes associated with mild head trauma.


Evaluation of cognitive assessment and cognitive intervention for people with multiple sclerosis
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Objectives: Cognitive problems in multiple sclerosis are common but any possible benefits of treatment remain uncertain. The aim of the study was to evaluate the benefits of providing a psychology service, including cognitive assessment and intervention, to patients with multiple sclerosis.

Method: The study was a single blind randomised controlled trial. A total of 240 patients with clinically definite, laboratory supported, or clinically probable multiple sclerosis were recruited from an multiple sclerosis management clinic and assessed on a brief screening battery. They were randomised into three groups. The control group received no further intervention. The assessment group received a detailed cognitive assessment, the result of which was fed back to staff involved in the patients' care. The treatment group received the same detailed cognitive assessment and a treatment programme designed to help reduce the impact of their cognitive problems. Patients were followed up 4 and 8 months later on the general health questionnaire (GHQ-28), extended activities of daily living scale, SF-36, everyday memory questionnaire, dysexecutive syndrome questionnaire, and memory aids questionnaire.

Results: The three groups were compared on the outcome measures at 4 and 8 months after recruitment. There were few significant differences between the groups and those that occurred favoured the control group. Overall, the results showed no effect of the interventions on mood, quality of life, subjective cognitive impairment or independence.

Conclusions: The study failed to detect any significant effects of cognitive assessment or cognitive intervention in this cohort of people with multiple sclerosis.
Diagnostic criteria and the use of ICD-10 codes to define and classify minor head injury

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Background: Epidemiological research on the incidence of traumatic head injuries relies on the correct definition and classification of the injury.

Objective: To address the use of diagnostic criteria and ICD-10 codes to define minor head injury in Swedish hospitals managing patients with head injury.

Methods: A questionnaire was mailed to all 76 Swedish hospitals managing head injuries. The hospitals were asked what diagnostic criteria they use to define minor head injury, and which ICD-10 codes they use to classify such injuries.

Results: 72 hospitals (95%) responded to the survey. The most common criterion was loss of consciousness (76%), followed by post-traumatic amnesia (38%). Almost half the hospitals used other signs and symptoms to define minor head injury. The ICD-10 code S.06 (intracranial injury) was used by 51 of the hospitals (91%).

Conclusions: It is essential that there should be common definitions, classifications, and registration of minor head injuries. The wide variation in definition and classification found in this study emphasises the importance of improved implementation of the present guidelines.

Respiratory aspects of neurological disease

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Neurological disease may result in respiratory dysfunction; however the manifestations of respiratory dysfunction in such patients may be atypical because of wider effects of their underlying condition. In the present review we have considered separately acute neuromuscular respiratory disease (as well as aspects of respiratory muscle function relevant to intensive care), chronic neuromuscular respiratory disease, sleep related disorders, respiratory consequences of specific neurological diseases, and neurological features of respiratory disease. Approaches to specific clinical problems are discussed; in many instances this can be expedited by close cooperation with a respiratory physician. We suggest that management of respiratory dysfunction in neurological disease depends critically on three factors: firstly, knowledge of when respiratory
dysfunction is likely to occur; secondly, maintaining a high index of clinical suspicion (specifically apparently vague symptoms should not be uncritically attributed to the underlying neurological condition); and, thirdly, the pursuing of appropriate investigations.

**Natural history of mild cognitive impairment in older persons**

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**Background:** Cognitive abilities of older persons range from normal, to mild cognitive impairment, to dementia. Few large longitudinal studies have compared the natural history of mild cognitive impairment with similar persons without cognitive impairment.

**Methods:** Participants were older Catholic clergy without dementia, 211 with mild cognitive impairment and 587 without cognitive impairment, who underwent annual clinical evaluation for AD and an assessment of different cognitive abilities. Cognitive performance tests were summarized to yield a composite measure of global cognitive function and separate summary measures of episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability. The authors compared the risk of death, risk of incident AD, and rates of change in global cognition and different cognitive domains among persons with mild cognitive impairment to those without cognitive impairment. All models controlled for age, sex, and education.

**Results:** On average, persons with mild cognitive impairment had significantly lower scores at baseline in all cognitive domains. Over an average of 4.5 years of follow-up, 30% of persons with mild cognitive impairment died, a rate 1.7 times higher than those without cognitive impairment (95% CI, 1.2 to 2.5). In addition, 64 (34%) persons with mild cognitive impairment developed AD, a rate 3.1 times higher than those without cognitive impairment (95% CI, 2.1 to 4.5). Finally, persons with mild cognitive impairment declined significantly faster on measures of episodic memory, semantic memory, and perceptual speed, but not on measures of working memory or visuospatial ability, as compared with persons without cognitive impairment.

**Conclusions:** Mild cognitive impairment is associated with an increased risk of death and incident AD, and a greater rate of decline in selected cognitive abilities.
Evidence for a separate type of migraine with aura
Sporadic hemiplegic migraine
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Objective: To compare clinical characteristics of patients with sporadic hemiplegic migraine (SHM) with those of patients with migraine with typical aura (MA) and patients with familial hemiplegic migraine (FHM).

Methods: The authors used a computer search of Denmark’s National Patient Register to screen the population for patients with migraine with aura with motor weakness, and also examined case records from headache clinics and private practicing neurologists and placed advertisements. The authors screened patients and their relatives with a semi-structured validated telephone interview. All recruited patients were then interviewed by a physician and given a neurologic examination.

Results: A total of 105 patients with SHM were identified. Seventy-two percent had four typical aura symptoms: visual, sensory, aphasic, and motor. All had at least two symptoms present during SHM attacks. A gradual progression and sequential appearance of aura symptoms was typical; compared with MA, the duration of each aura symptom was usually prolonged and bilateral motor symptoms were more frequent. Of the patients with SHM, 72% fulfilled the criteria for basilar migraine during SHM attacks. The aura was usually followed by headache, as is common in FHM but not MA.

Conclusions: Patients with sporadic hemiplegic migraine had clinical symptoms identical to familial hemiplegic migraine and significantly different from migraine with typical aura. Sporadic hemiplegic migraine is a separate entity, and should be classified with familial hemiplegic migraine.

Impaired financial abilities in mild cognitive impairment
A direct assessment approach
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Objectives: To assess financial capacity in patients with mild cognitive impairment (MCI) using a standardized psychometric capacity measure.
Methods: Participants were 21 cognitively normal older controls, 21 patients with amnestic MCI, and 22 patients with mild AD. The Financial Capacity Instrument (FCI), a psychometric capacity measure consisting of 18 financial ability tests (tasks), 9 domains (activities), and 2 total scores, was administered to participants along with a battery of neuropsychological tests sensitive to dementia. Group differences were examined on the neuropsychological and financial capacity variables.

Results: Relative to controls, the MCI group demonstrated impairments in episodic memory, and also semantic knowledge, executive function, written arithmetic, and spatial attention. MCI participants demonstrated impairments in FCI domains of conceptual knowledge, cash transactions, bank statement management, and bill payment, and in overall financial capacity. The control and MCI groups performed significantly better than patients with AD on most financial capacity and cognitive measures.

Conclusions: On direct assessment, patients with amnestic MCI as a group demonstrate impairments across a range of financial abilities. These impairments are mild and may only apply to a subset of patients with MCI. However, existing diagnostic criteria for MCI should be applied flexibly to include mild impairments in higher order activities of daily life such as financial capacity.

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Mild cognitive impairment in the oldest old
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Background: No data exist on whether the syndrome of amnestic mild cognitive impairment occurs in the oldest old, or if the relationships for functional status and neuropsychometric performance based on clinical diagnosis hold true in this age group.

Design/Methods: The authors performed comprehensive neurologic evaluations, neuropsychometric testing, and functional assessments on a sample of 90- to 100-year-old residents of Rochester, MN. Subjects were diagnosed as normal or with amnestic mild cognitive impairment (MCI) or dementia according to well-accepted criteria. Data on the following measures were collected and analyzed: Record of Independent Living (ROIL), Mini-Mental State Examination (MMSE), Dementia Rating Scale (DRS), Trailmaking Test (TMT), and modified version of the Free and Cued Selective Reminding Test (FCSRT).

Results: Data on 111 subjects (56 normal, 13 MCI, and 42 dementia) were analyzed. On the ROIL, functional capacity to carry out activities of daily living was worse for patients with dementia compared to patients with MCI and normal subjects, but did not differ between MCI and normal subjects. Scores on the MMSE, DRS, and TMT-A were worse in the dementia group compared to the normal group, and in the dementia group compared to MCI, but scores on these
measures for normal subjects compared to patients with MCI were not different. Scores on the FCSRT and memory subtest of the DRS showed differences among all three groups.

**Conclusion:** In spite of the advanced age of the cohort, the relationship between cognitive and functional performance and clinical diagnosis follows patterns previously described in younger samples of normal subjects, subjects with amnestic mild cognitive impairment, and subjects with dementia.

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**Monitoring the occurrence of emerging forms of Creutzfeldt-Jakob disease in the United States**

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Transmissible spongiform encephalopathies (TSEs) attracted increased attention in the mid-1980s because of the emergence among UK cattle of bovine spongiform encephalopathy (BSE), which has been shown to be transmitted to humans, causing a variant form of Creutzfeldt-Jakob disease (vCJD). The BSE outbreak has been reported in 19 European countries, Israel, and Japan, and human cases have so far been identified in four European countries, and more recently in a Canadian resident and a US resident who each lived in Britain during the BSE outbreak. To monitor the occurrence of emerging forms of CJD, such as vCJD, in the United States, the Centers for Disease Control and Prevention has been conducting surveillance for human TSEs through several mechanisms, including the establishment of the National Prion Disease Pathology Surveillance Center. Physicians are encouraged to maintain a high index of suspicion for vCJD and use the free services of the pathology center to assess the neuropathology of clinically diagnosed and suspected cases of CJD or other TSEs.

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**Neurologic manifestations of lightning strikes**

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Objective: To review neurologic sequelae of lightning strikes, to consider prevention and management, and to discuss current knowledge about the mechanism of lightning damage to tissues.

Results: Most lightning-related neurologic damage involves the CNS as opposed to the peripheral nervous system. The neurologic syndromes can be divided into the following four groups: immediate and transient, immediate and prolonged or permanent, delayed, and traumatic lesions secondary to falls and blast effects. Neurobehavioral complications are frequent and resemble the symptoms of patients with traumatic brain injury. Treatment of CNS lesions, such as posthypoxic encephalopathy and intracranial hemorrhages, is similar to that applied to patients with traumatic brain injury. Many patients with lightning strike are healthy, young individuals engaged in outdoor recreational activities. The mechanism of tissue injury is discussed.
Tests were made for use-dependent plasticity in the cholinergic projections to hippocampus. Transient infusion of the cholinergic agonist carbachol into hippocampal slices induced rhythmic activity that persisted for hours after washout. Comparable effects were obtained with physostigmine, a drug that blocks acetylcholine breakdown and thereby enhances cholinergic transmission. It thus seems that activation of cholinergic synapses induces lasting changes in hippocampal physiology. Two lines of evidence indicated that cholinergic synapses are also the sites at which the plasticity is expressed. First, the induction and expression of the rhythms were not blocked by the N-methyl-D-aspartate receptor antagonist D-2-amino-5-phosphonovaleric acid, indicating that a long-term potentiation effect between pyramidal cells was not involved. Second, a muscarinic antagonist (atropine) completely abolished stable rhythmic activity after agonist washout. This result indicates that endogenous cholinergic activity is responsible for the persistence of rhythmic oscillations. These experiments suggest that short periods of intense cholinergic activity induce lasting changes in cholinergic synapses and thus extend such forms of plasticity to beyond the glutamatergic system.

Shaken baby syndrome in Canada: clinical characteristics and outcomes of hospital cases
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Background
Shaken baby syndrome is an extremely serious form of abusive head trauma, the extent of which is unknown in Canada. Our objective was to describe, from a national perspective, the clinical characteristics and outcome of children admitted to hospital with shaken baby syndrome.

Methods
We performed a retrospective chart review, for the years 1988–1998, of the cases of shaken baby syndrome that were reported to the child protection teams of 11 pediatric tertiary care hospitals in Canada. Shaken baby syndrome was defined as any case reported at each institution of intracranial, intraocular or cervical spine injury resulting from a substantiated or suspected shaking, with or without impact, in children aged less than 5 years.

Results
The median age of subjects was 4.6 months (range 7 days to 58 months), and 56% were boys. Presenting complaints for the 364 children identified as having shaken baby syndrome were nonspecific (seizure-like episode [45%], decreased level of consciousness [43%] and respiratory difficulty [34%]), though bruising was noted on examination in 46%. A history and/or clinical evidence of previous maltreatment was noted in 220 children (60%), and 80 families (22%) had had previous involvement with child welfare authorities. As a direct result of the shaking, 69 children died (19%) and, of those who survived, 162 (55%) had ongoing neurological injury and
192 (65%) had visual impairment. Only 65 (22%) of those who survived were considered to show no signs of health or developmental impairment at the time of discharge.

Interpretation
Shaken baby syndrome results in an extremely high degree of mortality and morbidity. Ongoing care of these children places a substantial burden on the medical system, caregivers and society.

Addictive Behaviors
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Neuropsychological correlates of opioid dependence and withdrawal
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Severity of opioid dependence, and performance on two successive runs of the Wisconsin Card Sorting Test (WCST), were assessed in 39 right-handed male and female methadone patients who had been randomly assigned to either a recently dosed (n=21) or 24 hr abstinent (n=18) condition. Results indicated that severity of opioid dependence was positively correlated with perseverative responses and errors on the second run of the WCST, p<.05. Further, controlling for the effect of dependence severity, patients in early methadone withdrawal made selectively more perseverative responses and errors than did recently dosed patients, p<.05, with no difference on nonperseverative errors. **Findings were consistent with the hypothesis that opioid dependence, like alcoholism and cocaine addiction, is associated with disruption of executive cognitive functions mediated by the prefrontal cortex.**

The cognitive specificity of associative responses in patients with chronic pain
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Objective: Previous studies have found evidence of an associative response bias for patients with chronic pain. This body of research is not clear, however, on whether this bias is specific to patients with chronic pain, or whether the bias is specific to pain stimuli or illness/disability stimuli.

Design. This is a cross-sectional study involving the comparison of selected groups (chronic pain, acute pain, and medical-staff controls).
Method. This study included 80 male participants with chronic pain, 50 male participants with acute pain, and 49 male participants who served as medical staff controls. All participants completed the Beck Depression Inventory, the State-Trait Anxiety Inventory, a pain intensity VAS, and the single-word associate homographic response task.
Results. Evidence was found for the specificity of pain responses to homographic pain stimuli as the chronic pain group produced more of these responses than the two comparison groups.
Conclusions. These findings were seen as providing evidence for an associative response bias. This bias appears specific to pain-related stimuli and reflects the cumulative effects of pain over a period of time.

The relationship between illness attributions and attributional style in Chronic Fatigue Syndrome
Objective: To examine the relationship between illness attributions and general attributional style in Chronic Fatigue Syndrome (CFS).

Method. Participants with CFS answered questions on their explanation for their illness and completed the Attributional Style Questionnaire (parallel form).

Results. Of the participants, 58.3% attributed their illness to predominantly physical factors. A significant relationship was found between the presence of a self-serving attributional style and illness attributions.

Conclusion. Illness attributions were associated with an individual's general attributional style. It is suggested that illness attributions may be less important with regards prognosis than, for example, other variables which influence a person's general view of the world.

Social cognition in frontotemporal dementia and Huntington's disease

Frontotemporal dementia (FTD) and Huntington's disease (HD) are degenerative disorders, with predominant involvement, respectively of frontal neocortex and striatum. Both conditions give rise to altered social conduct and breakdown in interpersonal relationships, although the factors underlying these changes remain poorly defined. The study used tests of theory of mind (interpretation of cartoons and stories and judgement of preference based on eye gaze) to explore the ability of patients with FTD and HD to interpret social situations and ascribe mental states to others. Performance in the FTD group was severely impaired on all tasks, regardless of whether the test condition required attribution of a mental state. The HD group showed a milder impairment in cartoon and story interpretation, and normal preference judgements. Qualitative differences in performance were demonstrated between groups. FTD patients made more concrete, literal interpretations, whereas HD patients were more likely to misconstrue situations. The findings are interpreted as demonstrating impaired theory of mind in FTD, as one component of widespread executive deficits. In HD the evidence does not suggest a fundamental loss of theory of mind, but rather a tendency to draw faulty inferences from social situations. It is concluded that social breakdown in FTD and HD may have a different underlying basis and that the frontal neocortex and striatum have distinct contributions to social behaviour.
behavior. Previous studies carried out in the macaque monkey found that lesions of the amygdala not only decrease emotional reactivity but also disrupt normal social interactions. We have re-investigated the relationship between amygdala lesions and social behavior in cohorts of mature and neonatal rhesus monkeys who were prepared with selective and complete bilateral ibotenic acid lesions of the amygdaloid complex. These animals display clear alterations in emotional and social behavior. We interpret these changes as due to a loss of the ability to evaluate environmental stimuli as potential threats. However, adult animals with bilateral lesions of the amygdala demonstrate near normal, and even increased, social interactions with conspecifics. Moreover, neonatal animals, prepared with amygdala lesions at 2 weeks of age, also demonstrate species typical social behaviors such as the generation of facial expressions, grooming and play behavior. These results argue against the idea that the amygdala is essential for the interpretation of social communication or for the expression of social behavior. Because it does appear to participate in the evaluation of the "safety" of social interactions, we believe that it does have a role in modulating the amount of social behavior in which an organism will participate. However, our current answer to the question posed in the title of this paper is no!

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Motivation, reward, and Parkinson's disease: influence of dopatherapy
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"Orbitofrontal" and "cingulate" striatofrontal loops and the mesolimbic dopaminergic system that modulates their function have been implicated in motivation and sensitivity to reward in animals. Parkinson's disease (PD) provides a model to assess their implications in humans. The aims of the study were to investigate motivation and sensitivity to reinforcement in non-demented and -depressed PD patients and to evaluate the influence of dopaminergic therapy by comparing patients in "on" (with -Dopa) and "off" (without -Dopa) states. Twenty-three PD patients were compared, in both the "on" and "off" states, to 28 controls, using: (1) an Apathy Scale; (2) Stimulus–Reward Learning, Reversal, and Extinction tasks; and (3) a Gambling task. PD patients were found: (1) mildly apathetic; (2) impaired on Stimulus–Reward Learning and Reversal, but not on Extinction; and (3) able to progress in the Gambling task during the first, but not the second assessment. There was no significant correlation between these various deficits. -Dopa treatment clearly improved motivation, but had more limited and contrasting effects on other variables, decreasing the number of omission errors in Reversal, but increasing the number of perseveration errors in Extinction. These results suggest: (1) an implication of striatofrontal loops in human motivation and explicit and implicit sensitivity to reinforcement; (2) a positive influence of -Dopa treatment on the subjective evaluation of motivation, but contrasting effects on reward sensitivity.
ERPs and behavioural indices of long-term preattentive and attentive deficits after closed head injury
M. Dolores Polo, a, b, Phil Newtona, Danny Rogersa, Carles Escerab and Stuart Butlera

Attentional deficits are often reported even years after sustaining a closed head injury (CHI). Disturbance of cognitive attentional functions following CHI has been documented in both behavioural and event-related brain potential (ERP) studies. Recently, the possibility that the sequels of CHI extend to preattentive processes of attention has been pointed out. We used a paradigm that makes it possible to assess simultaneously the processing of relevant information and involuntary mechanisms of attention to gain further insight in this matter. Eleven patients with CHI greater than 1 year post-trauma and 14 age-matched control subjects were engaged in the performance of a continuous visual reaction time (RT) discrimination task while ignoring streams of auditory task-irrelevant stimuli. The main characteristic in the paradigm was that all visual stimuli were shortly preceded by an auditory stimulus, which could be a repeated (90%) or a different (deviant) tone. We measured performance on the discrimination task, and ERP indices of preattentive (mismatch negativity MMN) and attentive information processing (P1, N165, P3b). In relation to control subjects, CHI patients showed an attenuation of the MMN evoked by the deviant-tone. In response to the visual stimuli, CHI patients showed a delay of P1, and a reduction of the N165 and P3b components. Moreover, they had slower RT and missed more responses in a visual discrimination task. These results indicate both preattentive and attentive deficits, which is consistent with the typical diffuse axonal injury (DAI) resulting after CHI.

Effects of divided attention on episodic memory in chronic traumatic brain injury: a function of severity and strategy
Jennifer A. Mangels, a, Fergus I. M. Craikb, c, Brian Levineb, c, e, Michael L. Schwartzd, f and Donald T. Stussb, c, g

Eleven patients with mild traumatic brain injury (MTBI) and 13 patients with moderate-to-severe TBI (STBI) were compared to 10 matched controls on episodic memory for pictorial scene–object associations (e.g. kitchen–bread) and a range of standardized neuropsychological tests of memory and frontal-lobe functions. We tested the hypothesis that deficits in episodic memory result from impaired attentional resources and/or strategic control by manipulating attentional load at encoding (focused versus divided attention) and environmental support at retrieval (free recall and recalled cued by scene versus recognition of object and scene). Patients with TBI were disproportionately affected by the divided attention manipulation, but this effect was modulated by injury severity and encoding strategy. Overall, MTBI patients were impaired only when items were encoded under divided attention, indicating memory deficits that were secondary to deficits in the executive control. STBI patients could be differentiated into two distinct functional subgroups based on whether they favored a strategy of attending to the encoding or digit-monitoring task. The subgroup favoring the digit-monitoring task demonstrated deficits in the focused attention condition, and disproportionate memory
deficits in the divided attention condition. In contrast, the subgroup favoring the encoding task demonstrated intact performance across all memory measures, regardless of attentional load, and despite remarkable similarity to the other STBI subgroup on demographic, neuropsychological, and acute injury severity measures. We discuss these outcome differences in terms of the relationship between strategy and executive control and highlight the need for more sensitive anatomical and behavioral measurement at both acute and chronic stages of injury.

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Working memory and apolipoprotein E: What's the connection?
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Two robust findings in the Alzheimer's literature are that patients with Alzheimer's disease (AD) show executive function and primacy deficits. The present study examined whether we would find similar deficits when comparing two groups of middle-aged individuals who differed with respect to genetic risk for AD, based on their apolipoprotein E (APOE) genotype. All individuals were screened as normal on a battery of standardized cognitive measures. They were tested on the "Operation span task", which engages the central executive component of working memory [J. Exp. Psychol.: Gen. 128 (1999) 309, J. Exp. Psychol.: Gen. 126 (1997) 211, J. Mem. Language 39 (1998) 418] by dividing attention between processing math operations and remembering words. Individuals were grouped according to APOE genotype (4 carrier versus 4 non-carrier), matched on age and education, and their Total span and Primacy scores were compared. Despite having no overt symptoms of dementia or deficits on a series of standardized psychometric tests, the 4 carriers showed divided-attention and primacy deficits on the Operation span task, when compared to the 4 non-carriers. As a point of comparison, Primacy scores were extracted from the first trial of the "Buschke selective reminding task" [J. Verbal Learn. Verbal Behav. 12 (1973) 543] for these same individuals, and no group differences were found. The Buschke task is a list-learning task that does not require divided attention. These findings suggested that the 4 carriers were less able to divide their attention, when compared to the 4 non-carriers. The findings provide the first direct evidence for a relationship between APOE genotype and cognitive performance on measures of divided attention and primacy with non-demented individuals who showed no cognitive impairments on standardized measures.

Epilepsy and Behavior

The Electroencephalogram in Attention Deficit-Hyperactivity Disorder: Emphasis on Epileptiform Discharges.
Hughes JR, DeLeo AJ, Melyn MA.
This study dealt with the electroencephalograms (EEGs) of 176 children with attention deficit-hyperactivity disorder (ADHD). Of special interest were the patients who had in their EEG some type of spike activity (spike group), in contrast with those without such activity (control group). In the entire group, 27.8% were completely normal and an additional 18.8% had positive spikes as their only finding. Definite noncontroversial, epileptiform activity was seen in 30.1%, mainly focal (usually occipital or temporal), less often generalized, with bilaterally synchronous spike and waves complexes seen in 11 children. Extreme spindles or diffuse slow waves occurred only in the spike group (one exception in each) and slow wave abnormalities (mainly frontal or temporal), nearly always mild in degree, were seen mainly in the spike group. These different findings suggest that ADHD is a condition often with organic changes in the form of EEG abnormality, at times with epileptiform activity that could contribute to a deficit in attention or a plethora of movements.

Proton Magnetic Resonance Spectroscopy Investigation of the Right Frontal Lobe in Children With Attention-Deficit/Hyperactivity Disorder.
Yeo RA, Hill DE, Campbell RA, Vigil J, Petropoulos H, Hart B, Zamora L, Brooks WM.
OBJECTIVE To investigate neurometabolite concentrations in right prefrontal white matter in children with attention-deficit/hyperactivity disorder (ADHD) and relations of neurometabolites with attention skill and frontal anatomy.METHOD Single voxel proton magnetic resonance spectroscopy (H-MRS), quantitative morphometric analysis of left and right dorsolateral frontal volumes, and assessment of attentional problems with the Conners Continuous Performance Test were undertaken in 23 children (17 male) with ADHD (with no comorbid learning disabilities) and 24 matched controls (16 male).RESULTS No overall group differences were found for any neurometabolite. However, a group by sex interaction was noted for -acetylaspartate, such that girls with ADHD had especially low concentrations. Morphological analyses revealed smaller right (but not left) dorsolateral volumes in children with ADHD, and in the ADHD group this volume correlated with neurometabolite concentrations. In the ADHD group Continuous Performance Test performance was related to both dorsolateral volume and the creatine-phosphocreatine peak from H-MRS.CONCLUSIONS These results add to a growing body of evidence suggesting sex-specific neurobiological differences in ADHD and draw attention to relationships between neurochemistry, neuroanatomy, and performance in children with ADHD. Study limitations include small sample size and clinical heterogeneity among the children with ADHD.

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Development of the key behaviors change inventory: a traumatic brain injury behavioral outcome assessment instrument.
Kolitz BP, Vanderploeg RD, Curtiss G.
OBJECTIVE: To describe the development and initial validation of a neurobehavioral outcome measure, the Key Behaviors Change Inventory (KBCI), for individuals with traumatic brain injury (TBI). DESIGN: Scale construction and development, and validity study. SETTING: Large state university and postal survey. PARTICIPANTS: Seventy-five volunteer undergraduate students and 25 volunteer collateral informants of individuals with TBI participated in the item-analysis phase. Thirty members of the Brain Injury Association and 20 members of the National Multiple Sclerosis Society rated both an identified patient and an age- and gender-equated control in the validation phase. INTERVENTIONS: Not applicable. MAIN OUTCOME MEASURES: Content validity was examined through expert panel item sorts. Scale internal consistencies were examined with the Cronbach alpha. Construct validity was examined by comparing scale elevations between controls and 2 neurologic groups. RESULTS: Item-analysis procedures resulted in 8 scales of 8 items each: inattention, impulsivity, unawareness of problems, apathy, interpersonal difficulties, communication problems, somatic difficulties, and emotional adjustment. Internal consistency reliability coefficients ranged from .82 to .91. Multivariate analysis of variance revealed significant (P <= .001) differences in scale elevations among TBI, multiple sclerosis (MS), and control groups. The TBI and MS groups scored significantly higher than the control group on all scales; a subset of KBCI scales discriminated between the 2 neurologic groups. CONCLUSION: The KBCI was both sensitive and specific to typical behavioral changes after TBI, thus supporting its usefulness in rehabilitation settings. Cross-validation and development of a normative database are future steps necessary in its development.

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Attenuated Left Prefrontal Activation during a Verbal Fluency Task in Patients with Depression.
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Functional neuroimaging studies on patients with depression have found abnormal activity in the left prefrontal and anterior cingulate cortex compared with healthy controls. Other studies have shown that these regions become active in healthy subjects during verbal fluency tasks, while patients with depression show impaired performance on such tasks. We used functional magnetic resonance imaging to investigate changes in cerebral blood oxygenation associated with a verbal fluency task in depressed patients and healthy volunteers. In contrast to 10 age- and sex-matched healthy control subjects who activated the left prefrontal cortex and the anterior cingulate cortex during word generation, 10 depressed subjects showed attenuated activation in the left prefrontal cortex and did not show significant activation in the anterior cingulate cortex. These findings suggest that impaired performance during verbal fluency task in depressed patients is associated with abnormal neural responses within these regions.
Disruption of frontocerebellar circuitry and function in alcoholism.

This article represents a symposium of the 2002 joint meeting of RSA and ISBRA held in San Francisco. Presentations were Neuropathology of alcohol-related cerebellar damage in humans, by Antony J. Harding; Neuropathological evidence of cerebellar damage in an animal model of alcoholism, by Roberta Pentney and Cynthia Dlugos; Understanding cortical-cerebellar circuits through neuroimaging study of chronic alcoholics, by Peter R. Martin and Mitchell H. Parks; and Functional reorganization of the brain in alcoholism: neuroimaging evidence, by John E. Desmond, S.H. Annabel Chen, Michelle R. Pryor, Eve De Rosa, Adolf Pfefferbaum, and Edith V. Sullivan.

A critical discussion of the role of neuroimaging in mild cognitive impairment.
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OBJECTIVE: - In this paper, the current neuroimaging literature is reviewed with regard to characteristic findings in mild cognitive impairment (MCI). Particular attention is drawn to the possible value of neuroimaging modalities in the prediction and early diagnosis of Alzheimer's disease (AD). METHODS: - First, the potential contribution of neuroimaging to an early, preclinical diagnosis of degenerative disorders is discussed at the background of our knowledge about the pathogenesis of AD. Second, relevant neuroimaging studies focusing on MCI are explored and summarized. Neuroimaging studies were found through Medline search and by systematically checking through the bibliographies of relevant articles. RESULTS: - Structural volumetric magnetic resonance imaging (MRI) and positron emission tomography (PET)/single photon emission tomography (SPECT) are currently the most commonly used neuroimaging modalities in studies focusing on MCI. There were considerable variations in demographical and clinical characteristics across studies. However, significant hippocampal and entorhinal cortex volume reductions were consistently found in subjects with MCI as compared with cognitively unimpaired controls. While hippocampal and entorhinal cortex atrophy in subjects with MCI are also well-established risk factors for the development of AD, these measures cannot be regarded as being of high predictive value in an individual case. Evidence for other typical neuroimaging changes in MCI is still scarce. In PET and SPECT studies, reduced blood flow and/or glucose metabolism in temporoparietal association areas, posterior cingulate and hippocampus were associated with a higher risk of progressive cognitive decline in MCI. In quantitative electroencephalogram (QEEG), low beta, high theta, low alpha and slowed mean frequency were associated with development of dementia. CONCLUSIONS: - Existing studies suggest that
neuroimaging measures have the potential to become valuable tools in the early diagnosis of AD. To establish their value in routine use, larger studies, preferably with long prospective follow-up are needed.

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Relationship between neuropsychological and emotional functioning in severe chronic alcoholism.
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Previous studies of patients with severe chronic alcoholism have shown a high prevalence of emotional distress such as anxiety and depression, and neuropsychological impairments such as executive deficits, but few have examined the relationship between these disorders. We addressed this issue in 51 abstinent patients with histories of severe chronic alcoholism utilizing the Minnesota Multiphasic Personality Inventory (MMPI) and the Halstead-Reitan Neuropsychological Test Battery (HRNTB). Applying factor analysis to the MMPI clinical and validity scales, we derived four dimensions accounting for 78% of the available variance. We found that Factor 1, which loaded on most clinical scales of the MMPI, was significantly correlated (p <.01) with performance on the Halstead Category Test (HCT), a measure of executive functioning. Further, group analysis with MANOVA using HCT (impaired and nonimpaired) as the independent variable revealed a significant main effect for Factor 1 (p <.004), which was maintained and strengthened when age and education were controlled as covariates (p <.001). The results suggest a relationship between emotional distress and executive functioning as measured by the HCT, reflecting differing facets of frontal lobe dysfunction common to cognitive and affective domains in patients with severe chronic alcoholism.

Sleep and the endocrine system: new associations to old diseases.
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Sleep and sleep disorders play a prominent role in hormone regulation. Given that sleep disordered breathing (SDB) and diabetes mellitus (DM) are thought to result from obesity, it has been assumed that when the two coexist, the diabetes was caused by the obesity. However, new data has shed light on the effects that SDB, sleep deprivation, and snoring have on glucose regulation. It now appears that in addition to causing daytime drowsiness, cardiovascular disease, mood and memory disturbances, impotence, and car wrecks, obstructive sleep apnea (OSA) also promotes insulin resistance. Though data is still sketchy on the optimum management of coexisting DM and OSA, large-scale studies will most likely prove that homeostatic glucose control in patients with sleep apnea will require aggressive treatment of their SDB.

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An emerging body of evidence suggests that an increased prevalence of insulin abnormalities and insulin resistance in Alzheimer's disease may contribute to the disease pathophysiology and clinical symptoms. It has long been known that insulin is essential for energy metabolism in the periphery. In the past 2 decades, convergent findings have begun to demonstrate that insulin also plays a role in energy metabolism and other aspects of CNS function. Investigators reported 20 years ago that insulin and insulin receptors were densely but selectively expressed in the brain, including the medial temporal regions that support the formation of memory. It has recently been demonstrated that insulin-sensitive glucose transporters are localised to the same regions supporting memory and that insulin plays a role in memory functions. Collectively, these findings suggest that insulin may contribute to normal cognitive functioning and that insulin abnormalities may exacerbate cognitive impairments, such as those associated with Alzheimer's disease. Insulin may also play a role in regulating the amyloid precursor protein and its derivative beta-amyloid (Abeta), which is associated with senile plaques, a neuropathological hallmark of Alzheimer's disease. It has been proposed that insulin can accelerate the intracellular trafficking of Abeta and interfere with its degradation. These findings are consistent with the notion that insulin abnormalities may potentially influence levels of Abeta in the brains of patients with Alzheimer's disease. The increased occurrence of insulin resistance in Alzheimer's disease and the numerous mechanisms through which insulin may affect clinical and pathological aspects of the disease suggest that improving insulin effectiveness may have therapeutic benefit for patients with Alzheimer's disease. The thiazolidinedione rosiglitazone has been shown to have a potent insulin-sensitising action that appears to be mediated through the peroxisome proliferator-activated receptor-gamma (PPAR-gamma). PPAR-gamma agonists, such as rosiglitazone, also have anti-inflammatory effects that may be of therapeutic benefit in patients with Alzheimer's disease. This review presents evidence suggesting that insulin resistance plays a role in the pathophysiology and clinical symptoms of Alzheimer's disease. Based on this evidence, we propose that treatment of insulin resistance may reduce the risk or retard the development of Alzheimer's disease.

Neurobiological bases for the relation between sleep and depression.

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The serotonergic system is involved in the regulation of sleep and wakefulness, its activity being at maximum during the awake state and minimum during sleep. In particular, the production of rapid eye movement (REM) sleep depends on the decrease of serotonergic tone.
in brain stem structures. Thus, serotoninergic compounds which increase this tone (such as antidepressants) induce inhibition of REM sleep. Depression is associated with a functional decrease of serotoninergic neurotransmission and with specific alterations of sleep, notably insomnia. Paradoxically, even though they complain of sleep loss, depressed patients exhibit significant mood improvement after one night of sleep deprivation. This antidepressant effect can be accounted for by the same serotoninergic mechanisms as those described for pharmacological treatments. Indeed, the therapeutic action of antidepressants such as selective serotonin reuptake inhibitors is thought to depend directly on the enhancement of central serotoninergic neurotransmission. Such enhancement is achieved through desensitization of serotoninergic autoreceptors, which results from chronic treatment with these compounds. Sleep deprivation also induces an activation of serotoninergic neurons due to prolonged wakefulness, and leads to similar serotoninergic adaptive processes. The common neurobiological mechanisms resulting from pharmacological antidepressant treatment and sleep deprivation suggest that sleep loss in some insomniac or in depressed patients might be an endogenous compensatory process which would be therapeutical rather than pathological. This proposal should open the way to new strategies in the treatment of depression.

The Journal of Psychiatry & Law 30/Fall 2002
The best interests of the village children
GREGORY DECLUE, PH.D., ABPP
This article tracks a practicing, forensic psychologist's efforts to develop a scientifically based framework for doing child custody evaluations. To apply knowledge from the field of developmental psychology to questions considered by the courts, a search was made for an empirically validated list of effective parenting behaviors. Contrary, to expectations, no such list was found. A new developmental theory, group socialization theory, suggests that this is because parents are much less influential than has been assumed. Implications for child custody evaluators are explored. Other psychologists, particularly child development researchers, are encouraged to comment.

Multidisciplinary rehabilitation for people with Parkinson’s disease: a randomised controlled study
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Objective: To determine whether a programme of multidisciplinary rehabilitation and group support achieves sustained benefit for people with Parkinson’s disease or their carers. Methods: The study was a randomised controlled crossover trial comparing patients and carers who had received rehabilitation four months before assessment with those who had not. Patients were recruited from a neurology clinic, attended a day hospital from home weekly for six weeks using private car or hospital transport, and received group educational activities and individual
rehabilitation from a multidisciplinary team. Patients were assessed at entry and at six months using a 25 item self assessment Parkinson’s disease disability questionnaire, Euroqol-5d, SF-36, PDQ-39, hospital anxiety and depression scale, and timed stand-walk-sit test. Carers were assessed using the carer strain index and Euroqol-5d.

Results: 144 people with Parkinson’s disease without severe cognitive losses and able to travel to hospital were registered (seven were duplicate registrations); 94 had assessments at baseline and six months. Repeated measures analysis of variance comparing patients at the 24 week crossover point showed that those receiving rehabilitation had a trend towards better stand-walk-sit score (p = 0.093) and worse general and mental health (p = 0.002, p = 0.019). Carers of treated patients had a trend towards more strain (p = 0.086). Analysis comparing patients before and six months after treatment showed worsening in disability, quality of life, and carer strain.

Conclusions: Patients with Parkinson’s disease decline significantly over six months, but a short spell of multidisciplinary rehabilitation may improve mobility. Follow up treatments may be needed to maintain any benefit.

Headache 2003 Mar;43(3):245-50

Biofeedback-assisted relaxation in migraine headache: relationship to cerebral blood flow velocity in the middle cerebral artery.

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Objective.-To determine if migraineurs with aura respond differently to biofeedback/relaxation than those without aura and, if so, whether the variability in outcome can be explained by blood flow velocity. Background.-The relationship between cerebral blood flow velocity and treatment response to biofeedback/relaxation in migraine with and without aura is uncertain. Method.-Twenty migraineurs underwent 12 sessions of biofeedback/relaxation therapy, while 20 controls simply were told to relax on their own. Cerebral blood flow velocity was measured bilaterally in the middle cerebral artery with transcranial Doppler. Results.-The biofeedback group showed significant (P <.05) reductions in pain, depression, and anxiety compared to the control group. Patients with and without aura did equally well. There were significant (P <.05) left to right blood flow velocity differences only in the migraine with aura group. Maximum blood flow velocities were significantly higher (P <.05) in the migraine with aura group than in the cohort without aura. There was an inverse correlation between indicators of anxiety and blood flow velocity, perhaps related to hyperventilation-induced constriction in the small vessels distal to the middle cerebral artery. Conclusion.-The positive treatment response to biofeedback/relaxation in migraine headache is not related to presence of aura, nor to changes in blood flow velocity, but may be associated with reduction in anxiety and depression.

Neuropsychological Rehabilitation, 13, 1-2, 2003, 1 - 11

Brain injury and emotion: An overview to a special issue on biopsychosocial approaches in neurorehabilitation (SPECIAL ISSUE)

Williams A1, Evans A2
Survivors of acquired brain injury (ABI) are at risk of a range of neuropsychiatric and behavioural disorders. Emotional disturbance, with reactive elements of mood disorder, such as depression and anxiety, appear particularly common. Specific anxiety disorders, such as post-
traumatic stress disorder (PTSD) have also been identified. Pain syndromes are also commonly
particularly in those who have suffered Traumatic Brain Injuries (TBI). Survivors of ABI are
often at risk of substance misuse and of irritability states. Their relationships may suffer from the
stresses triggered by the aftermath of injury. Intimate, in particular, sexual relationships may be
particularly affected. These effects are not, necessarily, only consequent of severe injuries, as
mild TBI can also have, for some, significant neuropsychiatric effects. Assessment and
management of such conditions are compromised by survivors of injury often having a limited
insight into the sequelae of their injuries. Interventions for such disorders and forms of distress
are increasingly available. This paper introduces the special issue of Neuropsychological
Rehabilitation on biopsychosocial approaches in neurorehabilitation. A range of papers provide
overviews for assessing and managing such neuropsychiatric, mood and behavioural (health and
habit) disorders.

Psychological adjustment, social enablement and community integration following
acquired brain injury
Philip J. Yates A1
Understanding and facilitating the process of psychological adjustment to acquired disability
arising from brain injury continues to pose a considerable challenge to rehabilitation
professionals. This paper reviews the literature on psychological adjustment to acquired
disability and chronic health conditions as they may be applied to acquired brain injury. It is
proposed that services are developed that address the psychosocial issues faced by survivors of
brain injury. Case illustrations are provided that demonstrate a process of adjustment and
integration towards participation in meaningful roles within the community.

Neurorehabilitation and cognitive-behaviour therapy of anxiety disorders after brain
injury: An overview and a case illustration of obsessive-compulsive disorder
W. H. Williams A1, J. J. Evans A2, S. Fleminger A3
Survivors of acquired and traumatic brain injuries may often experience anxiety states.
Psychological reactions to neurological trauma may be caused by a complex interaction of a host
of factors. We explore how anxiety states may be understood in terms of a biopsychosocial
formulation of such factors. We also review the current evidence for the presence of specific
anxiety disorders after brain injury. We then describe how cognitive-behaviour therapy (CBT), a
treatment of choice for many anxiety disorders, may be integrated with cognitive rehabilitation
(CR), for the management of anxiety disorders in brain injury. We illustrate how CBT and CR
may be delivered with a case of a survivor of traumatic brain injury (TBI) who had developed
obsessive compulsive disorder and health anxiety. We show how CBT plus CR allows a
biopsychosocial formulation to be developed of the survivor's concerns for guiding a goal-
based intervention. The survivor made significant gains from intervention in terms of goals
achieved and changes on clinical measures. We argue that large-scale research is needed
for developing an evidence base for managing emotional disorders in brain injury.
Neuropsychological Rehabilitation, 13, 1-2, 2003, 13 - 29

The three vectors of consciousness and their disturbances after brain injury
George P. Prigatano A1, Sterling C. Johnson A1

Based on the recent review of Zeman (2001) three "vectors" of consciousness are described. A model for understanding how they are related is outlined. Recent behavioural and neuroimaging studies are reviewed pertinent to this conceptualisation. Initial ideas for working with these disturbances in consciousness during neuropsychological rehabilitation are presented.

Neuropsychological Rehabilitation, 13, 1-2, 2003, 149 - 164

Tom M. McMillan A1, W. Huw Williams A2, Richard Bryant A3

In this paper we explore the evidence for post-traumatic stress disorder (PTSD) after traumatic brain injury (TBI). We examine its possible mediating mechanisms after brain injury, the evidence for its occurrence, risk, and protective factors, and the implications for intervention and service demands. In the first section we review the current literature relevant to cause, maintenance, and treatment of PTSD in general, before addressing issues associated with the assessment and management of PTSD after TBI. It is argued that PTSD may occur after a brain injury, and can be, relatively, a common disorder. However, explanatory mechanisms for its occurrence may be speculative. In this context, we argue, assessment and treatment need to be carefully considered, and comprehensive.

Neuropsychological Rehabilitation, 13, 1-2, 2003, 43 - 64

Impact of pre-injury factors on outcome after severe traumatic brain injury: Does post-traumatic personality change represent an exacerbation of premorbid traits?
Robyn L. Tate A1

Although personality change is a frequent and disabling consequence of severe degrees of traumatic brain injury (TBI), little information is available beyond descriptive statements. The present paper presents a brief overview of the literature on the effects of pre-injury variables on post-trauma psychosocial functioning, and makes specific examination of the effect of premorbid personality structure on the post-trauma personality in people with TBI. A close relative of 28 people undergoing rehabilitation after TBI completed the Eysenck Personality Questionnaire Revised (EPQ-R) and Current Behaviour Scale (CBS) regarding the injured person's personality and character. Data were collected on three occasions: Ratings about premorbid status were taken as soon as feasible after admission, and follow-up ratings regarding current status were made at 6 and 12 months post-trauma. As a group, premorbid ratings indicated an unremarkable profile on the EPQ-R. Significant changes had occurred by 6 months post-trauma, which were sustained at 12 months post-trauma for both the EPQ-R and CBS. Yet none of the specific hypotheses regarding premorbid personality structure on the EPQ-R and post-trauma
characterological deficits on the two CBS factors, Loss of Emotional Control (LEC) and Loss of Motivation (LM), was supported: There were no significant differences between subgroups with high or low premorbid levels of Extraversion, Neuroticism, Psychoticism, Addiction and Criminality and post-trauma CBS factors, LEC, and LM. These findings suggest that although personality changes occur as a result of traumatic brain injury, they are largely independent of the premorbid personality structure.

International Review of Psychiatry
12, 2, 2000, 157 - 169
Preventing disability from chronic pain: a review and reappraisal
Gerald M. Aronoff, Jeffrey B. Feldman
Chronic pain and disability are closely related. Evidence supporting the role of the central nervous system (cortical and limbic system), as opposed to peripheral, nociceptive processes, in the development and maintenance of chronic pain is reviewed. This includes the phenomenon of central sensitization, relevant limbic-cortical processes, and psychiatric diagnoses often co-morbid with chronic pain. Psychological and socioeconomic 'red flags' for a poor return to work prognosis are delineated. The critical importance of cognitive beliefs and, therefore, physician statements to patients concerning their medical condition, resulting restrictions, and limitations is emphasized. The relationship between motivation, performance, and patients' beliefs about what they can do (self-efficacy) and what will happen when they return to work is discussed. The need for a comprehensive interdisciplinary approach oriented towards functional restoration to enable patients with chronic pain to reach maximum medical improvement (MMI) is reviewed. It is argued that psychiatry, with a bio-psychosocial perspective is uniquely qualified to evaluate and treat chronic pain.

Neuropsychological Rehabilitation, 13, 1-2, 2003, 241 - 258
Episodic disorders of behaviour and affect after acquired brain injury
Peter Eames Eames A1, Rodger Ll. Wood A2
Psychological disorders that follow traumatic brain injury are possibly more complex and diverse than those associated with other forms of "brain damage". These may include organic aggressive, or organic affective syndromes that are episodic in nature and therefore require a more specific diagnosis, a different classification, and a different approach to treatment. Consequently, it is necessary for clinicians to learn to distinguish between "primary" psychiatric illnesses and those disorders of behavioural control and mood that stem specifically from brain injury. There is relatively little in the clinical literature that explains the relationship between variable states of behaviour, mood or temperament, and clinical disorders that may have long-term implications for patient management. This concept paper therefore addresses abnormalities of mood and behaviour that are episodic in character and are not recognisably included in the DSM and ICD classifications of psychological or psychiatric disorders.
Mild traumatic brain injury: Impairment and disability assessment caveats
Nathan D. Zasler A1, Michael F. Martelli A2
Mild traumatic brain injury (MTBI) accounts for approximately 80% of all brain injuries, and persistent sequelae can impede physical, emotional, social, marital, vocational, and avocational functioning. Evaluation of impairment and disability following MTBI typically can involve such contexts as social security disability application, personal injury litigation, worker's compensation claims, disability insurance policy application, other health care insurance policy coverage issues, and the determination of vocational and occupational competencies and limitations. MTBI is still poorly understood and impairment and disability assessment in MTBI can present a significant diagnostic challenge. There are currently no ideal systems for rating impairment and disability for MTBI residua. As a result, medicolegal examiners and clinicians must necessarily familiarise themselves with the variety of disability and impairment evaluation protocols and understand their limitations. The current paper reviews recommended procedures and potential obstacles and confounding issues.

Contemporary approaches to the management of irritability and aggression following traumatic brain injury
Nick Alderman A1
In this paper, the principal means of managing irritability and aggression following traumatic brain injury (TBI) will be briefly reviewed. The paper will initially consider the prevalence of irritability, what it is and some of the likely causes that drive the condition. Aggression will then be similarly contemplated. Prior to a discussion regarding those methods most regularly employed in their management, the attention of the reader will be directed to a range of methodological issues that need to be considered in relation to reporting treatment efficacy, including lack of homogeneity and the need to use standardised assessment tools. Three principal management approaches will then be described and appraised, these being pharmacology, psychotherapy, and behaviour therapy. Within the discussion of psychotherapeutic methods, special mention will be made with regard to use of cognitive behaviour therapy, and two detailed case studies will be employed to illustrate issues relating to both cognitive behaviour therapy and behaviour therapy.

Pain following traumatic brain injury: Assessment and management
Stephen Tyrer A1, Amy Lievesley A1
Traumatic brain injury is frequently associated with painful complaints immediately after injury and subsequently. Early assessment of possible painful conditions can be made at the time of physical examination in those who are unable to give a history. Non-verbal signs of pain, including withdrawal of a painful limb or body part, irritability or tears should draw the attention
of the assessing physician to a peripheral painful site. Treatment of conditions giving rise to pain can be made at this stage. Persistent pain may arise from a combination of physical and psychological factors and is best managed in a multidisciplinary pain clinic. Contributions from physicians in pain management, psychologists, physiotherapists and clinical nurse specialists enable a rehabilitation programme to take place. Treatments include analgesic drugs, graded exercise, cognitive-behavioural therapy, and transcutaneous electrical nerve stimulation. Rehabilitation of people who have a head injury and pain takes longer than usual and separate pain management facilities should be developed for this population.

Cognitive Neuropsychiatry, 8, 1, 2003, 1 - 18
Neurorehabilitation for two cases of post-traumatic stress disorder following traumatic brain injury
W.H. Williams A1, J.J. Evans A2, B.A. Wilson A2
Introduction. We present two cases to illustrate the assessment and management of post-traumatic stress disorder (PtSD) in the context of traumatic brain injury (TBI). Case KE suffered a TBI in a road traffic accident (RTA) in which his girlfriend was killed. Case CM survived a penetrating neurological injury from a severe knife attack. Both suffered cognitive difficulties, primarily in attention and memory, and selective visual impairments, and had endured significant losses of social role. Method. Within a neurorehabilitation programme, goals were set regarding management of their cognitive difficulties for regaining social roles and for the management of their PtSD symptoms. Cognitive behavioural therapy (CBT) was provided for managing PtSD symptoms, which included use of a stress inoculation and graduated exposure to avoided situations and trauma re-experiences. Results. Both survivors reported significant improvements in managing mood state, and in redeveloping social roles. Objective measures confirmed significant gains from intervention. Conclusions. CBT, set within a neurorehabilitation programme, can lead to improvement in PtSD symptoms and psychosocial outcome in TBI survivors.

Cerebral Cortex, Vol. 13, No. 3, 265-273, March 2003
fMRI Evidence for an Organization of Prefrontal Cortex by Both Type of Process and Type of Information
Marcia K. Johnson, Carol L. Raye, Karen J. Mitchell, Erich J. Greene and Adam W. Anderson1
Departments of Psychology and
1 Diagnostic Radiology, Yale University, New Haven, CT 06520-8205, USA
Address correspondence to Marcia K. Johnson, Department of Psychology, Yale University, Box 208205, New Haven, CT 06520-8205, USA. Email: marcia.johnson@yale.edu.

Neuroimaging evidence is conflicting regarding whether human prefrontal cortex (PFC) shows functional organization by type of processes engaged or type of information processed. Most studies use complex working or long-term memory tasks requiring multiple processes and the combinations of processes recruited for different materials may vary. Using functional magnetic resonance imaging (fMRI) and simple tasks suggested by a component process
approach, we found activity in left PFC when participants thought about (refreshed) a just-seen item and in right PFC when participants noted whether an item had been presented previously. Furthermore, the distribution of activation in left or right PFC varied with type of information. Thus, at the component process level, PFC shows functional organization by both process and type of information.

Cognitive Neuropsychiatry 7, 3, 2002, 251 - 269

**Phantom limbs: The body in mind**

Peter W. Halligan

Introduction. Advances in our knowledge of corporeal awareness is not limited to patients with amputations, however, until recently, the study of "phantom limbs" was neglected by comparison with less common disorders of body perception. Method. Reasons for the neglect of this potentially informative and common condition are conspicuous by their absence in previous reviews. Over the past decade, however, experimental investigations of phantom limbs have revealed the dynamic neural processes that provide for both phantom and normal corporeal embodiment. Moreover, these findings helped to overturn widely held scientific assumptions regarding the extent of neural plasticity in the adult brain. Results. It is suggested that throughout medical history, the construct of "phantom limbs" posed a challenge to fundamental folk assumptions regarding the assumed relationship between body and mind. Conclusion. Reluctance to entertain the counter-intuitive phenomenon of a "limbless perception" contributed to the comparative neglect of this fascinating phenomenon until the late 20th century.

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MRI study of Asperger syndrome.

Do children with autism fail to process context?

Ethics of autism: What's wrong with dominant paradigms.

Autism; deficit in broadening spread of visual attention.

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J Neurol Neurosurg Psychiatry 2002 Dec;73(6):619-28
The internet.
Al-Shahi R, Sadler M, Rees G, Bateman D.
Department of Clinical Neurosciences, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK. Rustam.Al-Shahi@ed.ac.uk
The growing use of email and the world wide web (WWW), by the public, academics, and clinicians-as well as the increasing availability of high quality information on the WWW-make a working knowledge of the internet important. Although this article aims to enhance readers' existing use of the internet and medical resources on the WWW, it is also intelligible to someone unfamiliar with the internet. A web browser is one of the central pieces of software in modern computing: it is a window on the WWW, file transfer protocol sites, networked newsgroups, and your own computer's files. Effective use of the internet for professional purposes requires an understanding of the best strategies to search the WWW and the mechanisms for ensuring secure data transfer, as well as a compendium of online resources including journals, textbooks, medical portals, and sites providing high quality patient information. This article summarises these resources, available to incorporate into your web browser as downloadable "Favorites" or "Bookmarks" from www.jnnp.com, where there are also freely accessible hypertext links to the recommended sites.

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TALK -
Roanoke and NYATBI

massive state cuts now require nice rehabilitation counselors to cut, because maintaining there jobs requires they act like assholes, requires that client recognize that his impatience about suboptimal vocational rehabilitation services must be checked, lest they use this as an excuse to cut his services. That is, in a restrictive services environment, manifestations of unhappiness are being observed to clearly result in negative reactions....

DAVID H

I was hoping to avoid this one... but yes, documented ciguatera poisoning can be associated with fatigue and neurological problems.
I deliberately omitted that journal. It is a very pro-multiple chemical sensitivity and fringe journal. I don't think it has much credibility.

David Hartman, Ph.D., ABPN

----- Original Message ----- From: Gian Carlo Buoiano To: Neuropsychology Sent: Tuesday, February 18, 2003 8:41 PM Subject: [npsych] Re: Ciguatera fish poisoning

Dr. Kennedy,

I think you may be interested in the following paper.

You might also contact professor Racciatti at his email address.

GB.

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The Science of the total environment - 2001 Apr 10;270(1-3):27-31
Chronic fatigue syndrome following a toxic exposure.
Racciatti D, Vecchiet J, Ceccomancini A, Ricci F, Pizzigallo E.

I can see how the *theory of Qeeg might meet Daubert standards. I cannot for the life of me understand how any individual Qeeg scan would meet the standard, given secret unpublished norms and proprietary algorithms.

David E. Hartman, Ph.D., ABPN

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NYATBI TALK - IME

Kanter and Pain Eval...

Competency...APA Standards...

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Journal: Neuropsychologia
ISSN : 0028-3932
Volume : 41
Table of Contents:

Different brain mechanisms mediate two strategies in arithmetic: evidence from Event-Related brain Potentials
R. El Yagoubi, P. Lemaire, M. Besson
pp 855-862
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S002839320200180X&_version=1&md5=97070eaa970b1ce776ce0b388c7be958

Neural correlates of naming animals from their characteristic sounds
D. Tranel, H. Damasio, G.R. Eichhorn, T. Grabowski, L.L.B. Ponto, R.D. Hichwa
pp 847-854
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002233&_version=1&md5=b032f63b5245ebfdca65b73cf617acb3

Mixed emotions: alcoholics' impairments in the recognition of specific emotional facial expressions
J.M. Townshend, T. Duka
pp 773-782
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002841&_version=1&md5=fdfe809354926bdcd6ad88b6f8e0e

Hemispace differences in the visual perception of size in left hemiParkinson's disease
J.P. Harris, E.A. Atkinson, A.C. Lee, K. Nithi, M.S. Fowler
pp 795-807
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002853&_version=1&md5=3d073ded10c5e28db4b119af0953bcca

Effects of deep brain stimulation on prehensile movements in PD patients are less pronounced when external timing cues are provided
T. Schenk, B. Baur, U. Steude, K. Botzel
pp 783-794
Rapid extraction of emotional expression: evidence from evoked potential fields during brief presentation of face stimuli
E. Eger, A. Jedynak, T. Iwaki, W. Skrandies
pp 808-817
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002865&_version=1&md5=49b277572aceb97dfccf5617968abe20

Interhemispheric neural summation in the split brain: effects of stimulus colour and task
M. Roser, M.C. Corballis
pp 830-846
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002877&_version=1&md5=baa7f1f92ddeebe9481ea89c492643b5

Involvement of the medial temporal lobe in priming for new associations
J. Yang, X. Weng, L. Guan, P. Kuang, M. Zhang, W. Sun, S. Yu, K. Patterson
pp 818-829
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202002890&_version=1&md5=e05b1e0225e6b0f9dde7bf955ec143ab

Multiple patterns of writing disorders in dementia of the Alzheimer type and their evolution
C. Luzzatti, M. Laiacona, D. Agazzi
pp 759-772
Full text via ScienceDirect:
http://www.sciencedirect.com/science?_ob=GatewayURL&_origin=CONTENTS&_method=citationSearch&_piikey=S0028393202003287&_version=1&md5=a597e29a91d7628a2a77775747ce003e

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pp CO2
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Ph: 800-888-5858 ext. 21587
Fax: 877-883-3168
3/13/2003
Config Review...Not at line yet...could be today or tomorrow...went into review today...2-3 days to build it...work on Saturdays.....Omaha Nebraska

- Tom Bondurant: 278-8900
- Steve Velazquez Note...
- BOOK REVIEWS: LEARK and ANDY
- Billing
- JHTR research paper...Pain and TBI...
- Kay Dennis DVH Talk
• ROANOKE Talk
• ===========
• Stacy Burcin:
• Beth Aberth, 757-356-9076/ 356-0287?
• Dana Hamel: 320-4124
• Tom Watkins, Soc Worker, Tuckers: 323-8652
• Shannon Payne, Coord at Holly Brook, 553-3278.
• Valerie: Fax Wave request to her at 217-9413
• Kevin: 222-7844
• Jeff: 758-9706
• Richard: 370-4710
• DIV22 Rehab Stuff...
• Epperle Letter for Bob Davies
• C.W.: 556-3909

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Trends in Neurosciences
When neurons form memories [Research Focus]
Pascal Fries, Guillén Fernández and Ole Jensen
Although long-term memory is central among our cognitive functions, the search for a direct neurophysiological correlate to it has proven difficult. The formation of new memories depends on the hippocampus and adjacent cortex, but the final storage is thought to be in a widely distributed neocortical network. Recent experiments, using simultaneous recordings from hundreds of sites in monkey neocortex, have revealed the activation of such a distributed network – probably reflecting the consolidation of long-term memory storage.

Neuroendocrine–immune interactions [Research Focus]
Michael Harbuz
Trends in Endocrinology and Metabolism, 2003, 14:2:51-52
Over the past 15 years, the mechanisms by which the brain communicates with the immune system and the immune system with the brain have been elucidated. Increasingly, we are beginning to realize that cytokines within the brain are no scientific oddity, but rather are an important component of normal brain functioning. They are able to alter behaviour, memory, stress responses, brain injury and are increasingly being linked to psychiatric disorders. Hormones, peptides and neurotransmitters regulate the immune system. Understanding the complex interactions of these systems is a challenge for the 21st century.

The prefrontal cortex in sleep [Review]
Amir Muzur, Edward F. Pace-Schott and J. Allan Hobson
Experimental data indicate a role for the prefrontal cortex in mediating normal sleep physiology, dreaming and sleep-deprivation phenomena. During nonrandom-eye-movement (NREM) sleep, frontal cortical activity is characterized by the highest voltage and the slowest brain waves compared to other cortical regions. The differences between the self-awareness experienced in waking and its diminution in dreaming can be explained by deactivation of the dorsolateral prefrontal cortex during REM sleep. Here, we propose that this deactivation results from a direct inhibition of the dorsolateral prefrontal cortical neurons by acetylcholine, the release of which is enhanced during REM sleep. Sleep deprivation influences frontal executive functions in particular, which further emphasizes the sensitivity of the prefrontal cortex to sleep.

An emerging molecular and cellular framework for memory processing by the hippocampus [Opinion]
Gayle M. Wittenberg and Joe Z. Tsien
The hippocampus plays a central role in memory consolidation, a process for converting short-term memory into cortically stored, long-lasting memory in the mammalian brain. Here, we review recent data and discuss the 'synaptic re-entry reinforcement' (SRR) hypothesis, which can account for the role of the hippocampus in memory consolidation at both the molecular and systems levels. The central idea of the SRR hypothesis is that reactivation of neural ensembles in the hippocampus during the consolidation period results in multiple rounds of NMDA-receptor-
dependent synaptic reinforcement of the hippocampal memory traces created during initial learning. In addition, such reactivation and reinforcement processes permit the hippocampus to act as a 'coincidence regenerator', providing coordinated input that drives the coherent reactivation of cortical neurons, resulting in the progressive strengthening of cortical memory traces through reactivation of cortical NMDA receptors.

Trends in Neuroscience, 4 March 2003
Improving memory at the flick of a switch
4 March 2003 12:00 GMT by Sabine Louët

German researchers report that they can improve human memory by electrical stimulation of the brain's cortex. They achieved this by studying the electrophysiological conditions relevant for sleep-associated memory processing in humans. "This is the first experiment which we found to increase the memory performance," said Jan Born, director of the Institute of Neuroendocrinology at the University of Lübeck, in Germany. He presented his unpublished data at the Annual Meeting of the German Physiological Society in Bochum, Germany.

Born's team knew that sleep, especially the early period rich in slow wave sleep (SWS), is important for memory consolidation.

The researchers asked volunteers to learn word pairs and then, using electroencephalography (EEG), monitored their brain activity as they slept. This allowed the researchers to examine specific subsets of the sleep cycle, which is typically divided into various phases including SWS and rapid eye movement (REM).

Previous work had shown that "spindle activity," which occurs during SWS and is characterized by slow oscillations below 1 Hz, increases after an intense period of learning - indicating that it is clearly relevant for the reprocessing of memories during sleep, says Born.

The trouble is that "slow oscillations are difficult to record [with EEG]," notes Fernando Lopes da Silva, from the Section of Neurobiology at the University of Amsterdam in the Netherlands. Carrying out similar memory experiments using magnetoencephalography (MEG), for instance, would give a higher sensitivity, he suggests.

But despite the relatively low sensitivity of EEG, Born's team was able to measure the oscillations. They discovered that, at the transition to SWS, there is a direct one-on-one correlation between spindle activity, which represents the reprocessing of the material learned, and a strong DC potential shift of negative polarity in the brain.

This observation inspired Born's team to stimulate the human cortex by inducing a negative potential shift, which might to directly induce increased spindle activity. The idea worked. "We observed an increase in memory performance," Born said. Applying a DC-potential to the human scalp significantly enhanced the recall of memories for paired word associates. Hence, concludes Born, the negative DC potential shift could play a significant role in memory processing during SWS.

"It is a very positive development," said Derk-Jan Dijk, director of the Surrey Sleep Research Centre at the University of Surrey, who was also speaking at the conference. "It has been difficult to establish the function of sleep in the context of neuroscience cognitive psychology," he added.
But these results are "very preliminary," Born warned. "We cannot exclude that the effect of applying the DC potential to the scalp, although taking place during the first 20 minutes or so of a three-hour sleep period, continued till the time of [memory] testing," he said.

Previous studies have associated negative potentials with an increase in vigilance and attention during wake time. Higher attention levels rather than the presumed consolidation process of memory during sleep could therefore explain the improvement of memory.

"It is a difficult point to distinguish," said Lopes da Silva. Indeed, the difficulty comes from the interpretation of experiments which have to be designed in a way that allows researchers to pinpoint whether sleep actually did improve the memory or whether good results were just attributable to an increase in attention.

To confirm these results, Surrey University's Dijk suggests that additional experiments with a different protocol should be carried out. For instance, testing of learned material could be done the next day to ensure that the improvement does not come from the lasting effect of applying negative current on the cortex, but from actual memory consolidation. Born agrees: "By postponing the recall testing by another day, you are sure that sleep manipulation does not interfere with recall testing."

Dijk's own research has shown that spindle frequency and incidence also depends on the time of day and on biological rhythms. This could imply that memory may be also linked with the biological clock.

Pediatrics 2003 Mar;111(3):554-63

***Sleep and neurobehavioral characteristics of 5- to 7-year-old children with parentally reported symptoms of attention-deficit/hyperactivity disorder.

Kosair Children's Hospital Research Institute, and Division of Pediatric Sleep Medicine, Department of Pediatrics. Department of Psychological and Brain Sciences, University of Louisville, Louisville, Kentucky.

OBJECTIVES: This study examined the hypothesis that domains of neurobehavioral function would be selectively affected by sleep-disordered breathing (SDB). Therefore, we assessed potential relationships between objectively measured sleep disturbances and neurobehavioral function in children with reported symptoms of attention-deficit/hyperactivity disorder (ADHD) and also determined the incidence of snoring and other sleep problems in 5- to 7-year-old children in the local community and potential relationships to parental snoring and passive smoking. METHODS: Parents of 5- to 7-year-old children in public schools were surveyed about their child's sleeping habits using a validated questionnaire. The questionnaire also asked whether they believed their child to be hyperactive or have ADHD. Children with reported symptoms of ADHD and control children were randomly selected and invited to the Sleep Medicine Center for an overnight polysomnographic assessment and a battery of neurocognitive tests. RESULTS: The questionnaire response rate was 47.6% (n = 5728). Frequent and loud snoring was reported for 673 children (11.7%). Similarly, 418 (7.3%) children were reported to have hyperactivity/ADHD, 313 (76.5%) of which were boys. Eighty-three children with parentally reported symptoms of ADHD were invited for full evaluation at the Sleep Medicine Center together with 34 control children. After assessment with the Conners' Parent Rating Scale, 44 children were designated as having "significant" symptoms of ADHD, 27 as "mild,"
and 39 designated as "none" (controls). Overnight polysomnography indicated that obstructive sleep apnea was present in 5% of those with significant ADHD symptoms, 26% of those with mild symptoms, and 5% of those with no symptoms. In the cohort, no sleep variable accounted for more than a negligible proportion of the variance in domains of neurobehavioral function.

CONCLUSIONS: An unusually high prevalence of snoring was identified among a group of children designated as showing mild symptoms of ADHD based on the Conners' ADHD index identified from a community sample. However, whereas SDB is not more likely to occur among children with significant ADHD symptoms, it is significantly highly prevalent among children with mild hyperactive behaviors. Sleep studies further revealed that rapid eye movement disturbances are more likely to occur in children with significant symptoms, and they seem to impose significant but mild effects on daytime neurobehavioral functioning. We conclude that in children with significant symptoms of ADHD, the prevalence of SDB is not different from that of the general pediatric population and that rapid eye movement sleep in these children is disturbed and may contribute to the severity of their behavioral manifestations. Furthermore, SDB can lead to mild ADHD-like behaviors that can be readily misperceived and potentially delay the diagnosis and appropriate treatment.

Brain 2003 Feb;126(Pt 2):482-94

Anatomical correlates of dyslexia: frontal and cerebellar findings.
Eckert MA, Leonard CM, Richards TL, Aylward EH, Thomson J, Berninger VW.
Department of Neuroscience, McKnight Brain Institute of the University of Florida, Gainesville, FL 32610, USA. eckert@ufl.edu

In this study, we examined the neuroanatomy of dyslexic (14 males, four females) and control (19 males, 13 females) children in grades 4-6 from a family genetics study. The dyslexics had specific deficits in word reading relative to the population mean and verbal IQ, but did not have primary language or motor deficits. Measurements of the posterior temporal lobe, inferior frontal gyrus, cerebellum and whole brain were collected from MRI scans. The dyslexics exhibited significantly smaller right anterior lobes of the cerebellum, pars triangularis bilaterally, and brain volume. Measures of the right cerebellar anterior lobe and the left and right pars triangularis correctly classified 72% of the dyslexic subjects (94% of whom had a rapid automatic naming deficit) and 88% of the controls. The cerebellar anterior lobe and pars triangularis made significant contributions to the classification of subjects after controlling for brain volume. Correlational analyses showed that these neuroanatomical measurements were also significantly correlated with reading, spelling and language measures related to dyslexia. Age was not related to any anatomical variable. Results for the dyslexic children from the family genetics study are discussed with reference to dyslexic adults from a prior study, who were ascertained on the basis of a discrepancy between phonological coding and reading comprehension. The volume of the right anterior lobe of the cerebellum distinguished dyslexic from control participants in both studies. The cerebellum is one of the most consistent locations for structural differences between dyslexic and control participants in imaging studies. This study may be the first to show that anomalies in a cerebellar-frontal circuit are associated with rapid automatic naming and the double-deficit subtype of dyslexia.
Treating acute stress disorder following mild traumatic brain injury.
Bryant RA, Moulds M, Guthrie R, Nixon RD.
OBJECTIVE: Acute stress disorder permits early identification of trauma survivors who are at risk of developing chronic posttraumatic stress disorder (PTSD). This study aimed to prevent PTSD in people who developed acute stress disorder after a mild brain injury by early provision of cognitive behavior therapy. METHOD: Twenty-four civilian trauma survivors with acute stress disorder were given five individually administered sessions of either cognitive behavior therapy or supportive counseling within 2 weeks of their trauma. RESULTS: Fewer patients receiving cognitive behavior therapy than supportive counseling met criteria for PTSD at a posttreatment evaluation (8% versus 58%, respectively). There were also fewer cases of PTSD at a 6-month follow-up evaluation among those receiving cognitive behavior therapy (17%) than among those receiving supportive counseling (58%). Patients in the cognitive behavior therapy condition displayed less reexperiencing and avoidance symptoms at the follow-up evaluation than patients receiving supportive counseling. CONCLUSIONS: These findings suggest that PTSD following mild brain injury can be effectively prevented with early provision of cognitive behavior therapy.

Working memory and prefrontal cortex dysfunction: specificity to schizophrenia compared with major depression.
Barch DM, Sheline YI, Csernansky JG, Snyder AZ.
Psychology (DMB), St. Louis, Missouri, USA
A large number of studies suggest the presence of deficits in dorsolateral prefrontal cortex function during performance of working memory tasks in individuals with schizophrenia. However, working memory deficits may also present in other psychiatric disorders, such as major depression. It is not clear whether people with major depression also demonstrate impaired prefrontal activation during performance of working memory tasks. We used functional magnetic resonance imaging to assess the patterns of cortical activation associated with the performance of a 2-back version of the N-Back task (working memory) in 38 individuals with schizophrenia and 14 with major depression. We found significant group differences in the activation of dorsolateral prefrontal cortex associated with working memory performance. Consistent with prior research, participants with schizophrenia failed to show activation of right dorsolateral prefrontal cortex in response to working memory tasks demands, whereas those with major depression showed clear activation of right and left dorsolateral prefrontal cortex as well as bilateral activation of inferior and superior frontal cortex. During performance of working memory tasks, deficits in prefrontal activation, including dorsolateral regions, are more severe in participants with schizophrenia (most of whom were recently released outpatients) than in unmedicated outpatients with acute nonpsychotic major depression.
Association of comorbid posttraumatic stress disorder and major depression with greater risk for suicidal behavior.
Oquendo MA, Friend JM, Halberstam B, Brodsky BS, Burke AK, Grunebaum MF, Malone KM, Mann JJ.

OBJECTIVE: Posttraumatic stress disorder (PTSD) increases the risk of suicidal behavior; a major depressive episode also increases the risk for suicidal behavior. The authors' goal was to examine the effect of comorbid PTSD and major depressive episode on suicidal behavior.

METHOD: Inpatients with a diagnosis of major depressive episode (N=156) were assessed for PTSD, suicidal behavior, and clinical risk factors for suicidal acts. RESULTS: Patients with comorbid major depressive episode and PTSD were more likely to have attempted suicide, and women with both disorders were more likely to have attempted suicide than men with both disorders. Cluster B personality disorder and PTSD were independently related to history of suicide attempts. CONCLUSIONS: The greater rate of suicide attempts among patients with comorbid PTSD and major depressive episode was not due to differences in substance use, childhood abuse, or cluster B personality disorders.

Effects of expectations for different reward magnitudes on neuronal activity in primate striatum.
Cromwell HC, Schultz W.

In behavioral science, it is well known that humans and non-human animals are highly sensitive to differences in reward magnitude when choosing an outcome from a set of alternatives. We know that a realm of behavioral reactions is altered when animals begin to expect different levels of reward outcome. Our present aim was to investigate how the expectation for different magnitudes of reward influences behavior-related neurophysiology in the anterior striatum. In a spatial delayed response task, different instruction pictures are presented to the monkey. Each image represents a different magnitude of juice. By reaching to the spatial location where an instruction picture was presented, animals could receive the particular liquid amount designated by the stimulus. Reliable preferences in reward choice trials and differences in anticipatory licks, performance errors and reaction times indicated that animals differentially expected the various reward amounts predicted by the instruction cues. 374 of 2000 neurons in the anterior parts of the caudate nucleus, putamen and ventral striatum showed five forms of task-related activation during the preparation or execution of movement and activations preceding or following the liquid drop delivery. Approximately one-half of these striatal neurons showed differing response levels dependent upon the magnitude of liquid to be received. Results of a linear regression analysis showed that reward magnitude and single cell discharge rate were related in a subset of neurons by a monotonic positive or negative relationship. Overall, these data support the idea...
that the striatum utilizes expectancies that contain precise information concerning the predicted, forthcoming level of reward in directing general behavioral reactions.

Cognitive Impairment in Patients with Chronic Pain: The Significance of Stress
Robert P Hart PhD, James B Wade PhD and Michael F Martelli PhD
This review article examines the role of emotional distress and other aspects of suffering in the cognitive impairment that often is apparent in patients with chronic pain. Research suggests that pain-related negative emotions and stress potentially impact cognitive functioning independent of the effects of pain intensity. The anterior cingulate cortex is likely an integral component of the neural system that mediates the impact of pain-related distress on cognitive functions, such as the allocation of attentional resources. A maladaptive physiologic stress response is another plausible cause of cognitive impairment in patients with chronic pain, but a direct role for dysregulation of the hypothalamic-pituitary-adrenocortical axis has not been systematically investigated.

The influence of "State" related factors on focused attention following whiplash associated disorder.
Blokhorst M, Swinkels M, Lof O, Lousberg R, Zilvold G.
Roessingh Research and Development, Enschede, The Netherlands. m.blockhorst@rrd.nl
The modified Stroop task was presented to 48 patients with a Whiplash Associated Disorder (WAD) and 48 healthy matched controls to investigate possible attentional impairments in relation to state related factors (headache, neck pain, fatigue, tension and state-anxiety). It was expected that performance on the Stroop task is negatively influenced by these state related variables. Confirming the expectations, the results showed that response latencies increase for Subtasks 1 through 4, for both groups. In addition, WAD patients performed significantly worse on all subtasks. There was a significant interaction between the two groups and the four subtasks. The results revealed signs for interference susceptibility or reduced capacity to shift attention on the modified Stroop task. The results concerning the influence of state variables indicated that the intensity of headache was significantly related (demonstrating a worsening) to Stroop task performance in the WAD-group. It was concluded that WAD patients exhibit a general slowing of information processing, especially on tasks that require controlled attention. There are signs for subtle deficits in focused attention. The intensity of headache seems to play an important influence on attentional functioning. Clinical implications are discussed.
**Attentional functioning in fibromyalgia, rheumatoid arthritis, and musculoskeletal pain patients.**
Dick B, Eccleston C, Crombez G.
Dalhousie University/IWK Health Centre, Halifax, Nova Scotia, Canada.
OBJECTIVES: To investigate whether chronic pain patients have deficits in attentional functioning compared with pain-free controls, and whether fibromyalgia patients have larger deficits in attentional functioning compared with rheumatoid arthritis and musculoskeletal pain patients. METHODS: Sixty patients (20 in each of 3 patient groups) and 20 pain-free controls completed measures assessing pain intensity, mood, pain-related disability, somatic awareness, and catastrophic thinking about pain. Attentional functioning was assessed using an age-standardized, ecologically valid test battery. Analyses were made of between-group differences. RESULTS: Sixty percent of patients had at least one score in the clinical range of neuropsychological impairment, independent of demography and mood. Fibromyalgia patients were more anxious and somatically aware than rheumatoid arthritis or musculoskeletal pain patients, but did not show larger attentional deficits than other patient groups. CONCLUSION: All 3 groups of chronic pain patients, regardless of diagnosis, had impaired cognitive functioning on an ecologically sensitive neuropsychological test of everyday attention.

Neuroreport 2003 Mar 24;14(4):619-21
**Retrosplenial cortical activation in the fibromyalgia syndrome.**
Wik G, Fischer H, Bragee B, Kristianson M, Fredrikson M.
1Uppsala University PET-centre, Uppsala University, Uppsala 2ARC-Aging Research Center, Karolinska Institute and Stockholm University, Stockholm.
To study the CNS in chronic muscular pain typical of fibromyalgia we compared PET measures of regional cerebral blood flow (rCBF) in eight fibromyalgic patients and controls at rest. Higher rCBF for patients than controls was found bilaterally in the retrosplenial cortex. Lower rCBF for patients than controls were seen in the left frontal, temporal, parietal, and occipital cortices. The higher retrosplenial rCBF in patients than controls may reflect increased attention towards sub-noxious somatosensory signaling, and agrees with the notion that fibromyalgic pain reflects secondary hyperalgesia. The brain regions with lower rCBF in fibromyalgic patients than controls participate in the normal cognitive processing of pain, which may be dysfunctional in fibromyalgia.

J Pain Symptom Manage 2002 Dec;24(6):578-85
**Phantom pain and risk factors: a multivariate analysis.**
Dijkstra PU, Geertzen JH, Stewart R, van der Schans CP.
Pain Expertise Center, Groningen, The Netherlands.
Phantom pain has been given considerable attention in literature. Phantom pain reduces quality of life, and patients suffering from phantom pain make heavy use of the medical system. Many risk factors have been identified for phantom pain in univariate analyses, including phantom sensations, stump pain, pain prior to the amputation, cause of amputation, prosthesis use, and years elapsed since amputation. Multivariate analyses are lacking in the literature and, therefore, no estimation of an overall risk for phantom pain can be made. The aim of this study was to
analyze risk factors in a multivariate analysis in 536 subjects (19% upper limb amputees and 81% lower limb amputees). These subjects filled out a questionnaire in which the following items were assessed; side, date, level, and reason of amputation, pre-amputation pain, presence or absence of phantom pain, phantom sensations and or stump pain, and prosthesis use. The prevalence of phantom pain was 72% (95% CI: 68 to 76%) for the total group, 41% (95% CI: 31 to 51%) in upper limb amputees and 80% (95% CI: 76 to 83%) in lower limb amputees. The most important risk factors for phantom pain were "bilateral amputation" and "lower limb amputation." The risk for phantom pain ranged from 0.33 for a 10-year-old patient with a distal upper limb amputation to 0.99 for a subject of 80 years with a bilateral lower limb amputation of which one side is an above knee amputation.


Coping strategies and life satisfaction in subgrouped fibromyalgia patients.
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Department of Welfare and Care at Linkoping University, Faculty of Health Sciences, Norrkoping, Sweden. ragnhild.raak@ivv.liu.se
The present study describes pain- and stress-coping strategies and life satisfaction in subgroups of fibromyalgia patients. Thirty-two females with fibromyalgia syndrome (FMS) and 21 healthy pain-free women were studied. Those with FMS were classified as thermal (both heat and cold) pain sensitive or slightly cold pain sensitive based on pain thresholds determined using a Thermotest device. Global stress-coping styles, life satisfaction, and specific pain-coping strategies were measured. Patients classified as thermal pain sensitive were affected by physical symptoms to a greater extent than were those classified as slightly cold pain sensitive. The thermal pain sensitive group used more diverting attention coping strategies than the slightly cold pain sensitive group did. Separating fibromyalgia patients into subgroups might increase the potential for improving nursing care of these patients. Through the use of effective coping strategies in dealing with stress and pain, life satisfaction may also be enhanced.

Report
Chronic Nonmalignant Pain and Violent Behavior
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Abstract
Research suggests that violence has entered the medical setting to a remarkable degree, causing medical professionals to be at the highest risk for becoming the victims of assaults and violent acts. This article reviews general theories of aggression and research on these theories, and uses them to assess risk factors in patients with chronic pain. There are data to suggest that pain may increase the risk of aggressiveness in some patients. However, it may decrease the risk in others paradoxically. The research available underscores the need for evaluating patients with pain for the risk of violent or aggressive behavior; specific recommendations are made in this regard.

Report
Cluster Headaches and Sleep Disorders
Abstract
Cluster headaches are characterized by unilateral paroxysmal attacks of severe pain with associated symptoms. The headaches occur during particular sleep stages and are associated with other chronobiologic factors. Several sleep disorders have been associated with the occurrence of cluster headache; multiple hormonal influences affect the relationship between sleep and headache. Melatonin and other treatments that affect circadian rhythm have been suggested for the treatment of cluster headache. Obstructive sleep apnea can occur in patients with cluster headache; attempts to treat one disorder may influence the other. Sleep disorders such as insomnia and narcolepsy also may be associated with and influence cluster headaches. This article examines the relationship between the various sleep disorders and cluster headache, and reviews current research. Normal and abnormal sleep and details of treatments for specific sleep disorders that may decrease the frequency and severity of cluster headaches also are discussed. The relationship between obstructive sleep apnea, which is the most common sleep disorder, and cluster headache is discussed in detail.

Research article
Disability in young adults following major trauma: 5 year follow up of survivors
Sian A Evans1, Mark C Airey1, Susan M Chell1, James B Connelly1, Alan S Rigby2 and Alan Tennant3
Background
Injuries are a major cause of mortality and morbidity in young people. Despite this, the long-term consequences for young survivors of severe injury are relatively unexplored.
Methods
Population based cohort study involving 5 year post injury structured interview of all cases of major trauma (Injury Severity Score > 15) identified retrospectively for 12 month period (1988 to 1989) within former Yorkshire Health Authority area of the United Kingdom.
Results
125 individuals aged 11–24 years at time of injury were identified. Of these, 109 (87%) were interviewed. Only 20% (95% CI 14–29%) of those interviewed reported no disability. Mean Office of Population Census and Surveys (OPCS) disability score of the remainder was 7.5 (median 5.8, range 0.5 to 19.4). The most commonly encountered areas of disability were behaviour (54%, 95% CI 45–63%), intellectual functioning (39%, 95% CI 31–49%) and locomotion (29%, 95% CI 22–39%). Many respondents reported that their daily lives were adversely affected by their health problems for example, causing problems with work, 54% (95% CI 45–63%), or looking after the home, 28% (95% CI 21–38%). Higher OPCS scores were usually but not always associated with greater impact on daily activities. The burden of caring responsibilities fell largely on informal carers. 51% (95% CI 42–61%) of those interviewed would have liked additional help to cope with their injury and disability.
Conclusion
The study has revealed significant disability amongst a cohort of young people 5 years post severe injury. Whilst many of these young people were coping well with the consequences of
their injuries, others reported continuing problems with the activities of daily life. The factors underpinning the young people's differing experiences and social outcome should be explored

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The International Mail List for Pediatric Neuropsychologists. Subscribe by sending the message "subscribe ped-npsy [your first name] [your last name]" to listserv@tc.umn.edu (text must be in the message field, not the subject field).

Neurology 2003;60:1064-1070

**Why headache treatment fails**

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Management of headache disorders, a leading reason for neurologic outpatient visits, is often difficult. In this article, the authors summarize and categorize the common reasons for treatment failure leading to referral to subspecialty headache centers. They have grouped these treatment failures into five broad categories: 1) the diagnosis is incomplete or incorrect; 2) important exacerbating factors have been missed; 3) pharmacotherapy has been inadequate; 4) nonpharmacologic treatment has been inadequate; 5) other factors, including unrealistic expectations and comorbidity, exist. The authors present an orderly approach to treatment failure to assist neurologists in managing difficult patients. Most refractory headache patients have a biologically determined problem and can be helped by accurate diagnosis or effective treatment. Persistence in treating these patients can be very rewarding. The authors provide a checklist intended to facilitate the management of refractory patients

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**The role of APOE-4 in longitudinal cognitive decline**

MacArthur Studies of Successful Aging

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Background: While a genetic risk factor for late-onset AD, the effects of the 4 allele of the APOE gene on cognitive functioning more generally remain unclear.

Objective: To assess the role of the 4 allele of the APOE gene in longitudinal cognitive decline.

Methods: Multiple measures of cognitive function were assessed longitudinally in the MacArthur Successful Aging Study, a population-based cohort free of frank impairment at baseline. Subjects were 965 Caucasian and African American men and women from Durham NC, East Boston, MA, and New Haven, CT, aged 70 to 79 years, recruited in 1988 through 1989, who completed two follow-up evaluations, one at 3 years and another at 7 years.

Results: At the first follow-up, modest but significant declines in naming and spatial ability were associated with the APOE-4 genotype. By the second follow-up, more pronounced and significant associations were noted between the APOE-4 genotype and cognitive decline from six of the eight cognitive outcomes. After 7 years, APOE-4 allele carriers were twice as likely to have declined on a global cognitive score (odds ratio = 2.0; 95% CI: 1.1, 3.6) as noncarriers.

Conclusions: APOE-4 is associated with cognitive decline among a high-functioning elderly cohort, with effects most pronounced after 7 years of follow-up. Hence, the 4 allele either may function as a risk factor for cognitive impairment in normal aging across a broad spectrum of domains or may exert detectable effects early in a long prodromal AD trajectory.
twofold (OR 2.12; 95% CI 1.06 to 4.25). The odds of dementia increased by 2.67-fold for multiple infarctions (95% CI 1.08 to 6.61), whereas the odds of dementia with single infarctions increased by 69% (95% CI 0.70 to 4.09). In linear regression analyses, there was a trend for multiple infarctions to be associated with lower global cognitive scores (-0.44 standard units, p = 0.057). Multiple infarctions were related to perceptual speed, visuospatial skills, and working memory, but not to episodic or semantic memory. The authors found similar results with infarction volume. In secondary analyses, only infarctions that were clinically evident during life were associated with dementia and cognitive function.

Conclusion: Cerebral infarctions are associated with a twofold increase in odds of dementia. Odds are higher in persons with multiple, large, or clinically evident infarctions. In addition, cerebral infarctions do not affect all cognitive systems equally, showing the strongest association with perceptual speed and the weakest with episodic memory.

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Visual memory predicts Alzheimer’s disease more than a decade before diagnosis
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Background: Recent studies have suggested that AD may reflect a chronic process that begins many years before the clinical expression of dementia. The current study examines premorbid Benton Visual Retention Test (BVRT) and Wechsler Adult Intelligence Scale–vocabulary (WAIS-voc) test scores in order to determine whether long-term deficits in these tests can predict the development of AD decades later in the Baltimore Longitudinal Study of Aging (BLSA).

Method: Participants are volunteers from the BLSA, a multidisciplinary study of normal aging conducted by the National Institute on Aging. A total of 1,425 BLSA participants who were older than 60 years were included in the analyses. Cox proportional hazards models were used to estimate the relative risk of developing AD associated with BVRT and WAIS-voc scores at different time periods up to 20 years before the diagnosis of AD.

Results: The relative risks for 6 or more BVRT errors vs less than 6 errors at 1 to 3, 3 to 5, 5 to 10, and 10 to 15 years before the diagnosis of AD were 5.69, 2.11, 1.76, and 1.83 (p < 0.05). The relative risk for 15 or more years before diagnosis was not significant (p > 0.10). WAIS-voc scores were not significantly associated with the risk of AD in any time period.

Conclusions: A greater number of errors on the BVRT is associated with an increased risk of AD up to 15 years later. Poor visual memory performance may represent an early expression of AD years before diagnosis. This result suggests the need to continue to revise views on the natural history of AD and the possibility of an increased window of opportunity for preventive treatment before definitive diagnosis.
Caveats in the neuropsychological assessment of African Americans.
Department of Psychology, Howard University, Washington, DC 20059, USA.
This preliminary investigation examined the predictive accuracy of six neuropsychological tests in a population of non-brain-injured African Americans. False positives were unacceptably high on five of the neuropsychological tests administered. These pilot data raise important questions about the utility of neuropsychological test norms with groups dissimilar in sociocultural background to the normative population. These findings are examined in terms of the relative merits of the race-homogenous and race-comparative paradigms and underscore the importance of conducting normative studies that involve ethnic minority populations.

Facial recognition test in the elderly: norms, reliability and premorbid estimation.
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The Facial Recognition Test (Benton, Hamsher, Varney, & Spreen, 1983; Benton, Sivan, Hamsher, Varney, & Spreen, 1994) was examined in an age-, education- and gender-stratified sample of 346 healthy older adults. Internal consistency reliability estimates were .72 for the Long Form (FRLF), .53 for the Short Form, and .69 for a new short form. Mean FRLF scores did not change over a 1-year interval (p > .5), and the stability estimate was .71 (n = 100). The first of the methods below yielded the highest correlation between estimated and obtained FRLF scores in cross-validation (n = 67): (1) multiple regression based on oral reading and demographics, (2) multiple regression based on age, education and gender, and (3) mean scores by age group.

Mayo's Older Americans Normative Studies: expanded AVLT Recognition Trial norms for ages 57 to 98.
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This paper expands upon previously published Mayo's Older Americans Normative Studies (MOANS) Auditory Verbal Learning Test (AVLT) norms by presenting age and gender specific data for Recognition Trial accuracy (recognition 'hits' corrected for false positive errors) in a total of 836 subjects (the original sample, augmented by an additional 311 subjects).
Observations are offered concerning clinical implications of AVLT Recognition Trial performance. Gender differences in recognition memory are discussed.


**Computerized reaction time battery versus a traditional neuropsychological battery: detecting HIV-related impairments.**


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In recent years, interest in the use of computerized neuropsychological (NP) assessment measures has increased. However, there are limited data regarding how performance on these measures relates to performance on more traditional, clinical instruments. In the present study, 82 HIV+ men, who were all believed on clinical grounds to have neurobehavioral impairment, completed a traditional NP battery (TNB) and the California Computerized Assessment Package (CalCAP, a collection of computerized reaction time tests). Summary scores based on a TNB, as well as those based on the CalCAP, demonstrated significant associations with both degree of immunosuppression (CD4 count) and detectable viral load in cerebrospinal fluid, but not with detectable viral load in plasma. Established norms on the TNB and CalCAP batteries resulted in classifying 57% and 49% of the HIV+ sample as impaired, respectively. When using the TNB as the "gold standard," impairment classifications based on CalCAP summary scores exhibited a sensitivity of 68% and a specificity of 77%. Overall agreement on impairment classifications between batteries was low (kappa = .44). Data from this study suggest that traditional NP batteries and computerized reaction time tests do not measure the same thing, and are not interchangeable in examining HIV-related NP impairments.


**When the Third Party Observer of a Neuropsychological Evaluation is an Audio-Recorder.**

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The presence of third parties during neuropsychological evaluations is an issue of concern for contemporary neuropsychologists. Previous studies have reported that the presence of an observer during neuropsychological testing alters the performance of individuals under evaluation. The present study sought to investigate whether audio-recording affects the neuropsychological test performance of individuals in the same way that third party observation does. **In the presence of an audio-recorder the performance of the participants on memory tests declined. Performance on motor tests, on the other hand, was not affected by the presence of an audio-recorder.** The implications of these findings in forensic neuropsychological evaluations are discussed.
Post-Daubert admissibility of scientific evidence on malingering of cognitive deficits.
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In Daubert v. Merrell Dow Pharmaceuticals, Inc. (1993) the Supreme Court held that evidence must be "reliable" to be admissible and for scientific evidence "evidentiary reliability" is based on scientific validity. This article addresses the question "Do the Rey 15-Item Test ('FIT'), the Test of Memory Malingering ('TOMM'), and the Validity Indicator Profile ('VIP') likely meet the Daubert standard for admissibility of scientific evidence?" Sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and base rates of 30 and 15 percent were calculated for each test. Given the existing literature on malingering and the implications of a misclassification of malingering, we discuss the findings for each of the three tests using a PPV > or = 80 percent with a base rate of malingering of < or = 30. Our analyses indicate that the Rey 15-FIT fails to meet this standard of scientific validity. In contrast, the TOMM shows high specificity and PPV, and our findings suggest cautious optimism regarding the VIP. These results are discussed within the context of the courts' guidelines for the Daubert standard.

Neuroimaging of Hyperaroused and Dissociative States in Posttraumatic Stress Disorder
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Abstract: Posttraumatic stress disorder (PTSD) patients can have very different responses to recalling traumatic memories during neuroimaging. Pilot studies in our laboratory have shown that approximately 70 per cent of patients relived their traumatic experience and showed an increase in heart rate while recalling the traumatic memory. The other 30 per cent of patients had a dissociative response, with no concomitant increase in heart rate. The present paper reviews the neural correlates of these distinct responses. to elucidate which areas of the brain are involved in the recall of traumatic events.

To die or not to die for neurons in ischemia, traumatic brain injury and epilepsy: a review on the stress-activated signaling pathways and apoptotic pathways.
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After a severe episode of ischemia, traumatic brain injury (TBI) or epilepsy, it is typical to find necrotic cell death within the injury core. In addition, a substantial number of neurons in regions surrounding the injury core have been observed to die via the programmed cell death (PCD)
pathways due to secondary effects derived from the various types of insults. Apart from the cell loss in the injury core, cell death in regions surrounding the injury core may also contribute to significant losses in neurological functions. In fact, it is the injured neurons in these regions around the injury core that treatments are targeting to preserve. In this review, we present our cumulated understanding of stress-activated signaling pathways and apoptotic pathways in the research areas of ischemic injury, TBI and epilepsy and that gathered from concerted research efforts in oncology and other diseases. However, it is obvious that our understanding of these pathways in the context of acute brain injury is at its infancy stage and merits further investigation. Hopefully, this added research effort will provide a more detailed knowledge from which better therapeutic strategies can be developed to treat these acute brain injuries.

Emotional processing in personality disorder.
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In the field of personality disorders, borderline and antisocial types are associated with emotional dysfunctioning. In borderline personality disorder (BPD), the hypothesis of emotional hyperresponsiveness can be supported by several experimental studies that suggest highly intensive and slowly subsiding emotions to primed and non-primed stimuli, as well as by data showing biased information, which processes in the context of emotions. In addition, the first neuroimaging data suggest that limbic hypersensitivity is a neurofunctional correlate of emotional vulnerability in BPD. In antisocial psychopathic personality disorder, data confirm the theory of emotional detachment, subsuming fearlessness, and, beyond that, emotional indifference to appetitive stimuli. Because of a fundamental dysfunction in the amygdala, psychopathic individuals appear to use alternative cognitive operations of processing affective material to compensate for the absence of appropriate limbic input, which normally provides prompt information about the affective characteristics of stimuli.

Clin Neurophysiol 2003 Apr;114(4):673-84
Neural plasticity following auditory training in children with learning problems.
Hayes EA, Warrier CM, Nicol TG, Zecker SG, Kraus N.
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OBJECTIVE: This study examined the plasticity of the central auditory pathway and accompanying cognitive changes in children with learning problems.METHODS: Children diagnosed with a learning disability and/or attention deficit disorder worked with commercial auditory processing training software for 8 weeks; control groups consisted of normal-learning and learning-impaired children who did not participate in any remedial programs. Auditory brainstem function was evaluated in response to click and speech stimuli in quiet; cortical responses to speech stimuli were obtained in quiet and noise. Academic achievement and
cognitive abilities were assessed with standardized measures. RESULTS: Compared to controls, the trained group improved on measures of auditory processing and exhibited changes in cortical responses in quiet and in noise. In quiet, cortical responses reflected an accelerated maturational pattern; in background noise, cortical responses became more resistant to degradation. Brainstem responses did not change with training. CONCLUSIONS: Children with learning problems who practiced with auditory training software exhibited plasticity of neural encoding of speech sounds at the cortical, but not subcortical, level of the auditory pathway. This plasticity was accompanied by improvement in behavioral performance. SIGNIFICANCE: This study demonstrates that in learning-impaired children working with commercial auditory processing training programs affects both the perception and the cortical representation of sound.

Sleep 2003 Mar 15;26(2):117-26
The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation.
Van Dongen HP, Maislin G, Mullington JM, Dinges DF.
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OBJECTIVES: To inform the debate over whether human sleep can be chronically reduced without consequences, we conducted a dose-response chronic sleep restriction experiment in which waking neurobehavioral and sleep physiological functions were monitored and compared to those for total sleep deprivation. DESIGN: The chronic sleep restriction experiment involved randomization to one of three sleep doses (4 h, 6 h, or 8 h time in bed per night), which were maintained for 14 consecutive days. The total sleep deprivation experiment involved 3 nights without sleep (0 h time in bed). Each study also involved 3 baseline (pre-deprivation) days and 3 recovery days. SETTING: Both experiments were conducted under standardized laboratory conditions with continuous behavioral, physiological and medical monitoring. PARTICIPANTS: A total of n = 48 healthy adults (ages 21-38) participated in the experiments.
INTERVENTIONS: Nocturnal sleep periods were restricted to 8 h, 6 h or 4 h per day for 14 days, or to 0 h for 3 days. All other sleep was prohibited. RESULTS: Chronic restriction of sleep periods to 4 h or 6 h per night over 14 consecutive days resulted in significant cumulative, dose-dependent deficits in cognitive performance on all tasks. Subjective sleepiness ratings showed an acute response to sleep restriction but only small further increases on subsequent days, and did not significantly differentiate the 6 h and 4 h conditions. Polysomnographic variables and delta power in the non-REM sleep EEG—a putative marker of sleep homeostasis—displayed an acute response to sleep restriction with negligible further changes across the 14 restricted nights. Comparison of chronic sleep restriction to total sleep deprivation showed that the latter resulted in disproportionately large waking neurobehavioral and sleep delta power responses relative to how much sleep was lost. A statistical model revealed that, regardless of the mode of sleep deprivation, lapses in behavioral alertness were near-linearly related to the cumulative duration of wakefulness in excess of 15.84 h (s.e. 0.73 h). CONCLUSIONS: Since chronic restriction of sleep to 6 h or less per night produced cognitive performance deficits equivalent to up to 2 nights of total sleep deprivation, it appears that even relatively moderate sleep restriction
can seriously impair waking neurobehavioral functions in healthy adults. Sleepiness ratings suggest that subjects were largely unaware of these increasing cognitive deficits, which may explain why the impact of chronic sleep restriction on waking cognitive functions is often assumed to be benign. Physiological sleep responses to chronic restriction did not mirror waking neurobehavioral responses, but cumulative wakefulness in excess of a 15.84 h predicted performance lapses across all four experimental conditions. This suggests that sleep debt is perhaps best understood as resulting in additional wakefulness that has a neurobiological "cost" which accumulates over time.

T H I S W E E K ' S T O P A R T I C L E S

Does comorbid ADHD impact the clinical expression of pediatric OCD?

Responses to methylphenidate in ADHD and normal children

Non-stimulant treatment for ADHD.

Non-stimulant treatment of ADHD.

Psychopharmacologic strategies for the treatment of aggression in juveniles.

Forty years of methylphenidate treatment in ADHD.


EEG assessment of language function following stroke.

Detection Limit in Low-amplitude EEG Measurement.
Mind-body medicine: state of the science, implications for practice.
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BACKGROUND: Although emerging evidence during the past several decades suggests that psychosocial factors can directly influence both physiologic function and health outcomes, medicine had failed to move beyond the biomedical model, in part because of lack of exposure to the evidence base supporting the biopsychosocial model. The literature was reviewed to examine the efficacy of representative psychosocial-mind-body interventions, including relaxation, (cognitive) behavioral therapies, meditation, imagery, biofeedback, and hypnosis for several common clinical conditions.

METHODS: An electronic search was undertaken of the MEDLINE, PsycLIT, and the Cochrane Library databases and a manual search of the reference sections of relevant articles for related clinical trials and reviews of the literature. Studies examining mind-body interventions for psychological disorders were excluded. Owing to space limitations, studies examining more body-based therapies, such as yoga and tai chi chuan, were also not included. Data were extracted from relevant systematic reviews, meta-analyses, and randomized controlled trials.

RESULTS: Drawing principally from systematic reviews and meta-analyses, there is considerable evidence of efficacy for several mind-body therapies in the treatment of coronary artery disease (eg, cardiac rehabilitation), headaches, insomnia, incontinence, chronic low back pain, disease and treatment-related symptoms of cancer, and improving postsurgical outcomes. We found moderate evidence of efficacy for mind-body therapies in the areas of hypertension and arthritis. Additional research is required to clarify the relative efficacy of different mind-body therapies, factors (such as specific patient characteristics) that might predict more or less successful outcomes, and mechanisms of action. Research is also necessary to examine the cost offsets associated with mind-body therapies.

CONCLUSIONS: There is now considerable evidence that an array of mind-body therapies can be used as effective adjuncts to conventional medical treatment for a number of common clinical conditions.
External validity of a randomised clinical trial of temporomandibular disorders: analysis of the patients who refused to participate in research.
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PURPOSE: To assess the external validity of a randomised clinical trial (RCT) of a painful condition. METHOD: Consecutive patients with painful temporomandibular disorders (TMDs) were invited to participate in a clinical trial. Patients who refused to participate were compared to those who agreed to participate in this study with respect to degree of symptoms at time of presentation. RESULTS: The patients who refused to participate had more pain, and their condition interfered more with their daily life than those who accepted the invitation to participate. CONCLUSION: Selection bias in RCTs of painful conditions can skew the results, and external validity should be analysed before the results are generalised.

Peripheral and central mechanisms in tension-type headache: an update.
Jensen R.
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Despite the tremendous socioeconomic impact of tension-type headache surprisingly little is known about the underlying pathophysiology and treatment. Existing evidence and theories about the relation between central and peripheral mechanisms are discussed. Central sensitization is probably the most important key to understand this widespread disorder. An effective prevention or reversal of this central sensitization will probably be of major importance in future treatment strategies.

Relationship between pain and autonomic phenomena in headache and other pain conditions.
Janig W.
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Involvement of the (efferent) autonomic nervous system in the generation of pain is ongoing matter of debate. Based on clinical and experimental observations, there are good arguments that the sympathetic nervous system may be involved in pain following trauma, with and without nerve lesion, at an extremity, such as in complex regional pain syndrome type I and II. However, the mechanisms involved are in many cases still unclear. In various types of headache there is no convincing evidence that the sympathetic nervous system is involved in the generation of pain, although these pains may be accompanied by considerable autonomic reactions which are dependent on activity in sympathetic neurons. Migraine and headaches with autonomic symptoms are accompanied by autonomic reactions which are dependent on activity in cranial
parasympathetic neurons. **Whether parasympathetic neurons innervating cranial blood vessels are involved in activation or sensitization of trigemino-vascular afferents is discussed and needs experimental verification.**

Cephalalgia 2003 May;23 Suppl 1:13-31

**Electrophysiological studies in migraine: a comprehensive review of their interest and limitations.**
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Electrophysiological methods may help to unravel some of the pathophysiological mechanisms of migraine. **Lack of habituation is the principal and most reproducible interictal abnormality in sensory processing in migraineurs.** It is found in evoked potential (EP) studies for every stimulation modality including nociceptive stimuli, and it is likely to be responsible for the increased intensity dependence of EP. We have hypothesized that deficient EP habituation in migraine could be due to a reduced preactivation level of sensory cortices because of hypofunctioning subcortico-cortical aminergic pathways. This is not in keeping with simple hyperexcitability of the cortex, which has been suggested by some, but not all, studies of transcranial magnetic stimulation (TMS). A recent study of the effects of repetitive TMS on visual EP strongly supports the hypothesis that migraine is characterized by interictal cortical hypoexcitability. With regard to pain mechanisms in migraine, **electrophysiological studies of trigeminal pathways using nociceptive blink and corneal reflexes have confirmed that sensitization of central trigeminal nociceptors occurs during migraine attacks.**

Headache 2003 Apr;43(4):425-6

**Sensitization of trigeminal nociception specific for migraine but not pain of sinusitis.**
Katsarava Z, Lehnerdt G, Duda B, Ellrich J, Diener HC, Kaube H.
Neurology. 2002;59:1450-1453. Trigeminal pain processing was studied in 14 patients with unilateral migraine attacks and 14 age- and sex-matched patients with comparable unilateral headache from frontal sinusitis. Using a nociception-specific blink reflex method (nBR), a facilitation of nBR responses predominantly on the headache side was observed in migraine, but not in sinusitis. The facilitation of trigeminal nociception may be specific for migraine rather than a consequence of peripheral pain such as frontal sinusitis. Comment: Here we have evidence for the central hyperexcitability of migraine


**Cytokines, stress and depressive illness: brain-immune interactions.**
Anisman H, Merali Z.
Cytokines, signaling molecules of the immune system, have been implicated as a contributing factor for mood disorders such as depression. Several lines of evidence supporting this contention are briefly reviewed and caveats are introduced. Essentially, a relationship between cytokines and depression is based on the findings that: 1) proinflammatory cytokines (interleukin-1, interleukin-6, tumor necrosis factor-alpha) and bacterial endotoxins elicit sickness behaviors (e.g., fatigue, soporific effects) and symptoms of anxiety/depression that may be attenuated by chronic antidepressant treatment, 2) cytokines induce neuroendocrine and central neurotransmitter changes reminiscent of those implicated in depression, and these effects are exacerbated by stressors, 3) severe depressive illness is accompanied by signs of immune activation and by elevations of cytokine production or levels, and 4) immunotherapy, using interleukin-2 or interferon-alpha, promotes depressive symptoms that are attenuated by antidepressant treatment. It is argued that cytokine synthesis and release, elicited upon activation of the inflammatory response system, provoke neuroendocrine and brain neurotransmitter changes that are interpreted by the brain as being stressors, and contribute to the development of depression. Furthermore, such effects are subject to a sensitization effect so that a history of stressful experiences or cytokine activation augment the response to later challenges and hence the evolution of depression.

Clin Exp Allergy 2003 Apr;33(4):483-489
An association between plastic mattress covers and sheepskin underbedding use in infancy and house dust mite sensitization in childhood: a prospective study.
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BACKGROUND: Higher house dust mite (HDM) allergen exposure during infancy has been associated with increased HDM sensitization. Infant bedding has been associated with the accumulation of varying levels of HDM. Prospective data on the relationship between infant bedding and the development of HDM sensitization has not been previously examined.
OBJECTIVES: To determine if particular types of bedding used in infancy are associated with increased risk of house dust mite sensitization in childhood. METHODS: A population-based sample (n = 498) of children born in 1988 or 1989, and who were resident in Northern Tasmania in 1997, participated in this study. These children were part of a birth cohort study (1988-95), the Tasmanian Infant Health Survey. Data on infant underbedding and mattresses was available on 460 and 457 children, respectively. The main outcome measure was HDM sensitization defined as a skin prick test (SPT) reaction of 3 mm or more to the allergens of Dermatophagoides pteronyssinus and/or Dermatophagoides farinae. RESULTS: The use of either sheepskin underbedding or plastic mattress covers in infancy was associated with an increased risk of sensitization to HDM allergens at age 8 years. The adjusted risk ratio (RR) for sensitization to HDM with sheepskin in infancy was 2.27 (95% CI: 1.14, 4.55), P = 0.020. The adjusted RR for sensitization to HDM with the use of plastic mattress covers in infancy was 2.06 (95% CI: 1.22,
3.51), P = 0.007. The use of a foam mattress in infancy was not related to subsequent HDM sensitization. CONCLUSION: Infant's bedding plays a role in the development of HDM sensitization in childhood. Intervention studies to examine mite allergen levels and the role of underbedding on the development of HDM sensitization are required.

Brain Res 2003 May 2;971(1):73-82
Long-term sensitization of primary afferents in adult rats exposed to neonatal colon pain.
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We have previously shown that colon irritation (CI) in neonates results in chronic visceral hypersensitivity in adult rats, associated with central neuronal sensitization in the absence of identifiable peripheral pathology. The purpose of this study is to assess the relative contribution of peripheral mechanisms to chronic visceral hypersensitivity by examining the changes in responses of primary afferents at thoracolumbar (TL) and lumbosacral (LS) spinal segments to graded colorectal distension (CRD). Afferent discharges were recorded at the cut distal ends of spinal dorsal roots (DRs) in adult control and CI rats. We found that: (1) the average threshold of activation of LS afferents decreased significantly in CI rats; (2) the responses of TL and LS afferents to CRD in CI rats were significantly greater than those in control; (3) the spontaneous activity of LS afferents in CI rats was significantly stronger than that in control; (4) in CI rats, the average responses to graded CRD of LS DRs were significantly higher than those of TL DRs; and (5) the number of both LS DRs and TL DRs activated by CRD in CI rats was significantly larger than control. In summary, the results show that chronic visceral hypersensitivity is associated with peripheral sensitization, as well as central sensitization. TL visceral afferents projecting seem to be more involved in the processing of sensitized nociceptive input from the colon than acute nociceptive input. However, LS afferents seem to be equally important in both sensitized and acute pain states.

Brain Res 2003 May 2;971(1):55-65
Chronic cold stress sensitizes brain noradrenergic reactivity and noradrenergic facilitation of the HPA stress response in Wistar Kyoto rats.
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Many psychiatric disorders, including depression, post-traumatic stress disorder and other anxiety disorders, result from an interaction between genetic factors and exposure to a sufficiently sensitizing environmental stressor. The inbred Wistar Kyoto (WKY) rat strain has been proposed as a model of stress vulnerability, exhibiting an exaggerated hypothalamic-pituitary-adrenal (HPA) response to stress and susceptibility to gastric ulceration. Previously, we
showed that stress-activation of the brain noradrenergic system was deficient in WKY rats, and they lacked noradrenergic facilitation of the HPA response in the lateral bed nucleus of the stria terminalis (BSTL), compared to outbred Sprague-Dawley (SD) controls. Deficient modulatory function of the noradrenergic system may contribute to the stress susceptibility of WKY rats. Thus, we investigated the influence of a sensitizing stimulus, chronic intermittent cold exposure, on neuroendocrine and noradrenergic stress reactivity, and on noradrenergic facilitation of the HPA response in these two strains. Chronic cold exposure (7 days, 4 h/day, 4 degrees C) potentiated activation of the HPA axis by acute immobilization stress, assessed by measuring plasma adrenocorticotropic hormone (ACTH), in both strains, although to a greater extent in WKY rats, and enhanced stress-induced norepinephrine (NE) release in BSTL of WKY but not SD rats. We then compared the influence of chronic cold exposure on noradrenergic modulation of the HPA stress response in BSTL, by measuring changes in acute stress-induced elevation of plasma ACTH after microinjecting the alpha(1)-adrenoreceptor antagonist benoxathian into the BSTL. As shown previously, benoxathian attenuated stress-induced ACTH secretion in control SD but not control WKY rats. After chronic cold, the ACTH response to acute stress was attenuated by benoxathian administration into BSTL of both strains, such that the WKY response was not different from that of SD rats. Thus, chronic cold not only sensitized the release of NE in BSTL of WKY rats, but also restored noradrenergic facilitation of their already-elevated HPA response. Such functional sensitization of a previously-deficient facilitatory system may be one mechanism whereby exposure to repeated or severe stress may induce pathologic dysregulation of the stress response in susceptible individuals, resulting in psychiatric illness.

Brain Behav Immun 2003 Apr;17(2):86-93
Sensitization associated with stressors and cytokine treatments.
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Like stressors, interleukin-1beta and tumor necrosis factor-alpha (TNF-alpha) increase hypothalamic-pituitary-adrenal (HPA) activity and monoamine turnover at hypothalamic and extrahypothalamic sites. These effects can be re-elicited more readily upon reintroduction of these challenges (sensitization), depending on their time of re-exposure and the particular system being assessed. Following TNF-alpha administration, the co-expression of corticotropin releasing hormone (CRH) and arginine vasopressin increased within the median eminence, peaking 7-14 days after treatment, and was associated with an early corticosterone sensitization. However, the re-elicitation of sickness symptoms and corticosterone release was most pronounced at lengthy re-exposure intervals (28 days), possibly reflecting histamine release from mast cells. In addition, the cytokine engendered the sensitization of norepinephrine and serotonin utilization, and CRH immunoreactivity at mesocorticolimbic sites, but these effects were most prominent at brief re-exposure intervals (1-7 days). Cytokines may independently prime multiple regulatory systems, and by virtue of the neurochemical changes imparted, have both immediate and proactive influences on the evolution of psychopathology.
Temporal summation of pain from mechanical stimulation of muscle tissue in normal controls and subjects with fibromyalgia syndrome.

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Individuals diagnosed with fibromyalgia syndrome (FMS) report chronic pain that is frequently worsened by physical activity and improved by rest. Palpation of muscle and tendinous structures suggests that nociceptors in deep tissues are abnormally sensitive in FMS, but methods of controlled mechanical stimulation of muscles are needed to better characterize the sensitivity of deep tissues. Accordingly, force-controlled mechanical stimulation was applied to the flexor digitorum muscle of the forearm in a series of brief contacts (15 stimuli, each of 1s duration, at 3 or 5s interstimulus intervals). Repetitive stimulation was utilized to determine whether temporal summation of deep muscular pain would occur for normal subjects and would be enhanced for FMS subjects. Moderate temporal summation of deep pain was observed for normal controls (NC), and temporal summation was greatly exaggerated for FMS subjects. Temporal summation for FMS subjects occurred at substantially lower forces and at a lower frequency of stimulation. Furthermore, painful after-sensations were greater in amplitude and more prolonged for FMS subjects. These observations complement a previous demonstration that temporal summation of pain and after-sensations elicited by thermal stimulation of the skin are moderately enhanced for FMS subjects. Abnormal input from muscle nociceptors appears to underlie production of central sensitization in FMS that generalizes to input from cutaneous nociceptors.

Stress 2003 Feb;6(1):19-32

Stress and Cytokine-elicited Neuroendocrine and Neurotransmitter Sensitization: Implications for Depressive Illness.

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Stressful events, by their effects on neurotransmitter and neuroendocrine processes, are thought to favor the development or exacerbation of depressive illness. It is assumed that immunological challenge may precipitate stressor-like neuroendocrine and central neurochemical changes, thus promoting the evolution of affective illness. In this respect, viral and bacterial infections appear to influence behaviorally/metabolic (e.g. fever, anorexia, somnolence) and neurotransmitter functioning through the release of cytokines, which act as messengers between the immune system and brain. The present report provides a brief overview of the neurochemical consequences of proinflammatory cytokine treatments, particularly the actions of interleukin (IL)-1beta and tumor necrosis factor-alpha. As well, synergy with psychogenic and neurogenic stressors is described, as are data showing that cytokines, like stressors, may have time-dependent proactive (sensitization) effects, so that reexposure to the treatments greatly augments hypothalamic-
pituitary-adrenal activity, as well as central neurochemical changes. Indeed, the neurotransmitter alterations are not restricted to hypothalamic nuclei, but occur in several extrahypothalamic sites, including various limbic regions. It is suggested that by virtue of these neurochemical changes, cytokines may have both immediate and proactive effects on mood states.


'One-trial sensitization' to the anxiolytic-like effects of cannabinoid receptor antagonist SR141716A in the mouse elevated plus-maze.
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Significant variability in the effects of cannabinoid CB1 receptor ligands on emotional reactivity in animals and humans suggests that the endocannabinoid system may selectively modulate certain types of anxiety. In view of substantial evidence for qualitative differences in the nature of anxiety elicited on initial and subsequent exposures to the elevated plus-maze, the present studies contrasted the behavioural effects of the selective CB1 receptor antagonist SR141716A (0.1-10.0 mg/kg) and the reference benzodiazepine chlordiazepoxide (CDP, 15 mg/kg) both in maze-naive mice (trial 1) and in mice that had been given a single undrugged exposure to the maze 24 h prior to testing (trial 2). Results confirmed the anxioselective effect of CDP on trial 1 but a complete absence of such activity on trial 2 (i.e. one trial tolerance). In marked contrast, SR141716A had no behavioural effects in maze-naive mice but, at doses of 1.0-3.0 mg/kg (effect maximal at 1.0 mg/kg), significantly reduced anxiety-like responses in maze-experienced animals. Like the effect of CDP on trial 1, the antianxiety profile of SR141716A on plus-maze trial 2 was observed in the absence of any change in general activity levels. The apparent experientially induced 'sensitization' to the anxiolytic-like effects of SR141716A in the plus-maze contrasts markedly with the widely reported loss of benzodiazepine efficacy in test-experienced animals. Data are discussed in relation to the recently described phenotypes of CB1 receptor knockout mice and, in particular, to mounting evidence for the existence of a novel SR141716A-sensitive neuronal cannabinoid recepto

Toxicol Appl Pharmacol 2003 Apr 1;188(1):50-8

Acute stress modulates the irritant component of sensitizers in allergic contact dermatitis: implications for exposure assessment.
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Exposure of skin to noxious environmental stimuli can cause allergic contact dermatitis (ACD), which is a major health risk. Epidemiological studies have determined that 40% of workers
report that their jobs are very, or extremely, stressful, and the number of chemicals to which workers are exposed increases each year. We hypothesized that combined exposure to a workplace stressor and a sensitizing chemical would alter the time course and magnitude of the skin immune response. We assessed the mixed exposure of chemical and restraint stress using three potent skin sensitizers, 2,4 dinitrofluorobenzene (DNFB), dicyclohexylcarbodiimide (DCC), and oxazolone, (OXA) on the ear swelling response in stress-susceptible BALB/c mice. Quantitative analyses showed that the dose-response relationship for each chemical followed a cubic trend. Although stress did not alter the shape of the curve, application of restraint stress on day 1 or on day 6 diminished the ear swelling response to 0.1% DNFB. However, if the concentration of the challenge dose was increased to a more irritating concentration, 0.25% DNFB, ear swelling was enhanced. Restraint stress applied on day 6 also increased ear swelling in response to the highly irritating sensitizer DCC, but not to the low-irritancy chemical OXA. These data support the hypothesis that dose-response relationships exist for sensitization with chemical and that restraint stress modulation of the ear swelling response is both chemical specific and dependent on the irritancy potential of the chemical.

Predisposition to depression: the role of attachment.
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Suzanna Taryan, Consultant Child, Infant and Family PsychiatristMelbourne, Australia
Objective: To examine the hypothesis that adverse early relational experiences causing activation of the hypophysial-pituitary-adrenal (HPA) axis during critical early stages of development can predispose to depression. Patients thus affected are likely to manifest insecure patterns of attachment in close relationships and are vulnerable to depression after adverse life events.
Method: The literature pertaining to sensitization of the HPA axis in early life and the neurobiology of attachment is examined. Results: Adverse early relational experiences can result in activation of the HPA axis, causing sensitization of depression pathways in the brain. Secure attachment acts as a buffer against HPA activation in response to stress. Infants with insecure attachment lack this buffering effect and may be predisposed to depression and other psychiatric disorders in response to psychosocial stressors. Conclusions: There is a patient group predisposed to depression on the basis of adverse early life experience. In these cases, the neurobiology of attachment offers a means of integrating findings concerning sensitization of the HPA axis in infancy, the effects of early life experience on brain development, and predisposition to depression and other psychiatric disorders. These findings have important implications for the development of interventions aimed at prevention and treatment for this patient group.

Brain Behav Immun 2003 Feb;17(1 Suppl):119-24
Cytokines and depression: The need for a new paradigm.
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Considerable clinical and experimental data support the existence of a relationship between cytokines and depression. At the experimental level, proinflammatory cytokines have been found to induce alterations in brain function analogous to the behavioral and biological abnormalities occurring in depressed patients, including social withdrawal, cognitive impairment, anhedonia, increased activity of the hypothalamus-pituitary-adrenal axis, altered neurotransmission, and cross-sensitization with stressors. At the clinical level, the evidence in favor of innate immune system activation in depressed patients is still controversial, despite accumulating evidence for an increased risk of depressive disorders in patients receiving recombinant cytokines for the treatment of cancer and viral infection. This last issue has received significant attention recently, given that the administration of therapeutic cytokines provides a quasi-experimental model for studying the mechanisms which underlie the effects of cytokines on mood, cognition, and neurovegetative functions. Although the vulnerability factors that account for the risk of depression have yet to be identified, tryptophan depletion, likely related to the induction of indoleamine 2,3-dioxygenase enzyme, may represent an important mediator for the development of depressed mood in cytokine-treated patients. This paper discusses ways in which these emerging data may lead to advances in the recognition and management of non-specific neurobehavioral symptoms associated with the development and progression of cancer.

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The allocation of attention during locomotion is altered by anxiety
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Abstract We tested the hypotheses that: (1) anxiety regarding the possibility of falling alters the attentional demands of gait; and (2) this alteration in the attentional requirements of gait occurs independently of gait pattern accommodations. Sixteen younger and 15 older adults participated in this study. Subjects walked at a self-determined velocity along a 7.2-m walkway under four conditions of postural threat; the walking conditions varied depending on the width constraints of the walkway (60 cm vs 15 cm) and the height of the walking surface (0 cm vs 60 cm). Attentional demands of locomotion in each condition of testing were assessed using the dual-task methodology, in which participants verbally responded to an auditory cue as quickly as possible while continuing to walk. Our findings revealed that: (1) participants were successful in verbally responding to the auditory cue without modifying their gait pattern; (2) reaction times increased for all subjects when walking in the condition of greatest postural threat; (3) the attentional demands for locomotion varied with the phase of the gait cycle for younger adults but not for older adults; (4) the phase-dependent effect for younger adults disappeared in the condition of greatest postural threat, while reaction time scores for older adults systematically increased; and (5) increases in reaction time persisted despite significant changes in gait.
Our findings confirm that anxiety increases the attentional demands for locomotion and provide further explanation for age-dependent increases in the attentional demands of gait. Furthermore, our findings confirm that fall-related anxiety predicates an increase in the allocation of attention to locomotor control that is independent of gait pattern adjustments.

STUDY:

Forensic vs. Non, randomized counterbalanced design...

NEUROPSYCHOLOGY OF DEPRESSION

The neuropsychology of depression: a literature review and preliminary model.
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Neuropsychological research provides a useful framework to study emotional problems, such as depression, and their correlates. This paper reviews several prominent neuropsychological theories. Functional neuroanatomical systems of emotion and depression are reviewed, including those that describe cerebral asymmetries in emotional processing. Following the review, a model that is composed of three neuroanatomical divisions (left frontal, right frontal, and right posterior) and corresponding neuropsychological emotional sequelae within each quadrant is presented. It is proposed that dysfunction in any of these quadrants could lead to symptomatology consistent with a diagnosis of depression. The proposed model combines theories of arousal, lateralization, and functional cerebral space and lends itself to scientific methods of investigation. Accordingly, research, prevention, and treatment programs in accordance with the proposed model may promote a...
negative feedback; and (2) feedback and no-feedback versions of a computerised test of spatial working memory. In the feedback version, negative feedback was accurate, highly informative, and could be used as a mnemonic aid. RESULTS: On the Probability Reversal task, depressed patients were impaired in their ability to maintain response set in the face of misleading negative feedback as shown by their increased tendency to switch responding to the 'incorrect' stimulus following negative reinforcement, relative to that of controls. Patients' ability to acquire and reverse the necessary visual discrimination was unimpaired. On the Spatial Working Memory task, depressed patients made significantly more between-search errors than controls on the most difficult trials, but their ability to use negative feedback to facilitate performance remained intact. CONCLUSIONS: The present results suggest that feedback can have different effects in different contexts. Misleading, negative feedback appears to disrupt the performance of depressed patients, whereas negative but accurate feedback does not. These findings are considered in the context of recent studies on reinforcement systems and their associated neurobiological substrates.


Patterns of processing bias for emotional information across clinical disorders: a comparison of attention, memory, and prospective cognition in children and adolescents with depression, generalized anxiety, and posttraumatic stress disorder.

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This study investigated theoretical claims that different emotional disorders are associated with different patterns of cognitive bias, both in terms of the cognitive processes involved and the stimulus content that is preferentially processed. These claims were tested by comparing clinically anxious (generalized anxiety disorder [GAD], posttraumatic stress disorder [PTSD]) and clinically depressed children and adolescents on a range of cognitive tasks measuring attention, memory, and prospective cognition, with both threat-related and depressogenic stimulus materials. The results did reveal some relative specificity of processing in that the anxious participants exhibited a greater selective attentional bias for threat relative to depressogenic material with no such difference being apparent in the depressed sample. However, this bias was only clear-cut on a dot-probe measure of attentional processing and not on a modified Stroop measure, and indeed threat-related bias on the 2 tasks was uncorrelated. On the prospective cognition task, anxious participants exhibited an other-referent bias in their risk estimations regarding future negative events that was absent in the depressed sample. No specificity effects were evident on the memory task. The results are discussed in terms of the strengths and weaknesses of carrying out direct comparisons across groups and tasks versus drawing conclusions from overall patterns across multiple studies.

NEUROPSYCHOLOGY OF PAIN

J Clin Exp Neuropsychol 2002 Dec;24(8):994-1009
Controlled processes and automaticity in memory functioning in fibromyalgia patients: relation with emotional distress and hypervigilance.
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Evidence exists that chronic pain partially consumes the limited attentional resources, with the consequence that controlled processes sustaining cognitive tasks are affected and that automatic processes are preserved. Fibromyalgia syndrome is consistently rated as more severe than other chronic painful conditions. It is assumed here that fibromyalgia is more attention-demanding, leading to a more pronounced decrease of the controlled processes in comparison with other chronic painful conditions. In this perspective, Study 1 compares fibromyalgia patients, patients with localized pain and healthy subjects in a procedure separately estimating the within-task contributions of controlled and automatic processes in a cued recall task. As predicted, controlled processes are more strongly affected in fibromyalgia patients related to the group with localized pain. Unexpectedly, contribution of automatic processes is increased in fibromyalgia. Study 2 replicates these results and reveals that memory functioning in fibromyalgia patients is related to their painful condition as a whole rather than to any particular patient's characteristics.


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While characterization of pathogenetic mechanisms underlying major depression is a fundamental aim of neuroscience research, an equally critical clinical goal is to identify biomarkers that might improve diagnostic accuracy and guide treatment selection for individual patients. To this end, a synthesis of functional neuroimaging studies examining regional metabolic and blood flow changes in depression is presented in the context of a testable limbic-cortical network model. 'Network' dysfunction combined with active intrinsic compensatory processes is seen to explain the heterogeneity of depressive symptoms observed clinically, as well as variations in pretreatment scan patterns described experimentally. Furthermore, the synchronized modulation of these dysfunctional limbic-cortical pathways is considered critical for illness remission, regardless of treatment modality. Testing of response-specific functional relationships among regional 'nodes' within this network using multivariate approaches is discussed, with a perspective aimed at identifying biomarkers of treatment non-response, relapse risk and disease vulnerability. Characterization of adaptive and maladaptive functional interactions among these pathways is seen as a critical step towards future development of evidenced-based algorithms that will optimize the diagnosis and treatment of individual depressed patients.

Brain Behav Immun 2003 Apr;17(2):69-85
Bi-directional immune-brain communication: Implications for understanding stress, pain, and cognition.

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The immune system and the central nervous system form a bi-directional communication network. The critical roles of pro-inflammatory cytokines in both the periphery and the nervous system are discussed. In the periphery, these cytokines initiate the processes that signal the brain that immune activation has occurred, and communicate this information over both neural and blood-borne routes. The arrival of these signals in the central nervous system induces a neural cascade that includes the de novo induction of pro-inflammatory cytokines. The functions of these cytokines in the nervous system are discussed, and it is argued that they play a key role in regulating the neural control of immune processes in the periphery. In addition, it is argued that these cytokines play a variety of other roles, and some implications of the cytokine network for understanding stress, behavior, sensory processing, mood, and cognition are described. The overall argument is that because brain-mediated host defense involves behavioral, sensory, mood, and cognitive alterations, immune activation, and immune products such as the cytokines can have a pervasive effect on these functions. Finally, these phenomena are placed in an evolutionary perspective.

Brain Behav Immun 2003 Feb;17(1 Suppl):125-31

Immune-to-central nervous system communication and its role in modulating pain and cognition: Implications for cancer and cancer treatment.

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This paper reviews the nature of communication from the immune system to the brain and some implications of this communication for phenomena that are not ordinarily considered to be modulated by immune function. Pro-inflammatory cytokines released by activated immune cells signal the brain by both blood-borne and neural routes, leading to alterations in neural activity. The cascade of altered neural activity includes the induction of pro-inflammatory cytokines within the brain and spinal cord. The cytokines in the brain, specifically in the hippocampus, interfere with the consolidation of memory, while the cytokines within the spinal cord exaggerate pain. Activation of this immune-to-central nervous system pathway, with the consequent production of cytokines within the central nervous system, may be involved in the mediation of a number of phenomena that occur during cancer and cancer treatment.

Sommerfield, AJ; Deary, IJ; McAulay, V; Frier, BM (2003).
Moderate Hypoglycemia Impairs Multiple Memory Functions in Healthy Adults.
The effects of acute insulin-induced hypoglycemia on short-term, delayed, and working memory were examined in healthy adults. A hyperinsulinemic glucose clamp was used to maintain arterialized blood glucose at either 4.5 (euglycemia) or 2.5 (hypoglycemia) mmol/L on 2 separate occasions in 16 healthy volunteers. Tests of immediate and delayed verbal memory, immediate and delayed visual memory, and working memory were administered during each experimental condition. **All memory systems were impaired during acute hypoglycemia, with working memory and delayed memory being particularly susceptible. These findings are informative concerning the metabolic basis of adequate memory function and are of practical importance to people with insulin-treated diabetes, in whom hypoglycemia is common.**

Neurobiol Learn Mem 2002 Nov;78(3):578-95

**Stress and memory: opposing effects of glucocorticoids on memory consolidation and memory retrieval.**

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It is well established that glucocorticoid hormones, secreted by the adrenal cortex after a stressful event, influence cognitive performance. Some studies have found glucocorticoid-induced memory enhancement. However, many studies have reported impairing effects of glucocorticoids on memory function. This paper reviews recent findings from this laboratory on the acute effects of glucocorticoids in rats on specific memory phases, i.e., memory consolidation and memory retrieval. The evidence suggests that the consequences of glucocorticoid activation on cognition depend largely on the different memory phases investigated. Posttraining activation of glucocorticoid-sensitive pathways involving glucocorticoid receptors enhances memory consolidation in a pattern highly similar to that previously described for adrenal catecholamines. **Also, similar to catecholamine effects on memory consolidation, glucocorticoid influences on memory consolidation depend on noradrenergic activation of the basolateral complex of the amygdala and interactions with other brain regions. By contrast, memory retrieval processes are usually impaired with high circulating levels of glucocorticoids or following infusions of glucocorticoid receptor agonists into the hippocampus.** The hypothesis is proposed that these apparently dual effects of glucocorticoids on memory consolidation and memory retrieval might be related and that the basolateral complex of the amygdala is a key structure in a memory-modulatory system that regulates, in concert with other brain regions, stress and glucocorticoid effects on both memory consolidation and memory retrieval.

Journal of Clinical and Experimental Neuropsychology
2002 - volume 24 - issue 3, 335 - 355

**Neurophysiological and Clinical Aspects of Glucocorticoids and Memory: A Review**

Alderson, Amy L.; Novack, Thomas A.

Neuropsychologists are increasingly involved in the assessment and treatment of individuals with glucocorticoid (GC) dysfunction. This review examines the clinical and
neurophysiological changes associated with alterations in GC levels, with specific emphasis on changes in hippocampal plasticity and memory impairments. Hypothalamic-pituitary-adrenal (HPA) axis regulation of GC production and GC effects at hippocampal receptors are examined. GC-related changes in memory and hippocampal plasticity are considered in a wide array of populations, including animals, healthy adults, patients receiving exogenous GC treatments, and patients with neuropsychiatric disorders resulting in GC dysregulation. Hypotheses regarding GC-related memory changes are considered, with emphasis on hippocampal neurotoxicity and changes in excitatory amino acids, glucose metabolism and neurotrophic factors. These hypotheses are examined, with special attention given to inconsistencies and contradictions within this body of research. Finally, implications for neuropsychological evaluation and future research are presented.

Neurobiol Learn Mem 2002 Nov;78(3):570-7
Gene x environment interaction and cognitive performance: animal studies on the role of corticosterone.
de Kloet ER, Grootendorst J, Karssen AM, Oitzl MS.
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A fundamental question in the neurobiology of cognition is how stress and glucocorticoids modify learning and memory processes. Why some individuals develop cognitive deficits after stress, while other individuals improve in cognitive performance under similar adverse conditions is still unresolved. To address these questions we focus on those issues. First, corticosterone, which appears to be the preferred glucocorticoid for the rodent and human brain, acts via brain mineralocorticoid (MR) and glucocorticoid receptors (GR) on the expression of networks of corticosteroid-responsive genes. Different effects are achieved by MR and GR activation. Second, the experimental context that determines the timing and the consequences of corticosterone action during the various stages of information processing is reviewed. Third, the genetic context and the environmental context are investigated. Using apolipoprotein E knockout (apoE0/0) mice we show that apoE (apoE4 is a genetic risk factor for Alzheimer's disease) is a candidate gene with an important function in shaping the cognitive outcome (genotype x environment interaction)

Cytokines and cognition--the case for a head-to-toe inflammatory paradigm.
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The brain is not only immunologically active of its own accord, but also has complex peripheral immune interactions. Given the central role of cytokines in neuroimmunoendocrine processes, it is hypothesized that these molecules influence cognition via diverse mechanisms. Peripheral cytokines penetrate the blood-brain barrier directly via active transport mechanisms or indirectly via vagal nerve stimulation. Peripheral administration of certain cytokines as biological response modifiers produces adverse cognitive effects in animals and humans. There
is abundant evidence that inflammatory mechanisms within the central nervous system (CNS) contribute to cognitive impairment via cytokine-mediated interactions between neurons and glial cells. Cytokines mediate cellular mechanisms subserving cognition (e.g., cholinergic and dopaminergic pathways) and can modulate neuronal and glial cell function to facilitate neuronal regeneration or neurodegeneration. As such, there is a growing appreciation of the role of cytokine-mediated inflammatory processes in neurodegenerative diseases such as Alzheimer's disease and vascular dementia. Consistent with their involvement as mediators of bidirectional communication between the CNS and the peripheral immune system, cytokines play a key role in the hypothalamic-pituitary-adrenal axis activation seen in stress and depression. In addition, complex cognitive systems such as those that underlie religious beliefs, can modulate the effects of stress on the immune system. Indirect means by which peripheral or central cytokine dysregulation could affect cognition include impaired sleep regulation, micronutrient deficiency induced by appetite suppression, and an array of endocrine interactions. Given the multiple levels at which cytokines are capable of influencing cognition it is plausible that peripheral cytokine dysregulation with advancing age interacts with cognitive aging.

J Pers Assess 2003 Apr;80(2):139-51

The tripartite model of anxiety and depression: symptom structure in depressive and hypertensive patient groups.
Marshall GN, Sherbourne CD, Meredith LS, Camp P, Hays RD.
Health Program, RAND, Santa Monica, California.
The structure of self-reported symptoms representative of the tripartite model was examined using data drawn from the Medical Outcomes Study (Tarlov et al., 1989). Participants were persons who had been diagnosed 48 months previously as suffering from either depression (N = 315) or hypertension (N = 403). Results of confirmatory factor analyses were broadly consistent with the tripartite model (L. A. Clark & Watson, 1991). Factors emerged corresponding to each of the 3 posited first-order dimensions of negative affect, positive affect, and physiologic arousal. Nonetheless, some discrepancies were found between the observed data and the hypothesized tripartite model. First, the obtained physiologic arousal factor was best viewed as reflecting nonspecific somatic distress rather than physiologic arousal. Finally, although differentiable in the strictest statistical sense, all three domains were significantly correlated (.36 to .86, absolute value). In particular, contrary to the tripartite model, positive and negative affect covaried markedly (-.81 to -.86). Findings raise issues concerning the utility of the tripartite model as a heuristic framework for enhancing understanding of individual differences in normal mood as well as mood disorders.


Executive functions and their disorders.
Elliott R.
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The term executive function defines complex cognitive processing requiring the co-ordination of several subprocesses to achieve a particular goal. Neuropsychological evidence suggests that
executive processing is intimately connected with the intact function of the frontal cortices. Executive dysfunction has been associated with a range of disorders, and is generally attributed to structural or functional frontal pathology. Neuroimaging, with PET and fMRI, has confirmed the relationship; however, attempts to link specific aspects of executive functioning to discrete prefrontal foci have been inconclusive. Instead, the emerging view suggests that executive function is mediated by dynamic and flexible networks, that can be characterised using functional integration and effective connectivity analyses. This view is compatible with the clinical presentation of executive dysfunction associated with a range of pathologies, and also with evidence that recovery of executive function can occur after traumatic brain injury, perhaps due to functional reorganisation within executive networks.

Br Med Bull 2003;65:35-47
Emotion and its disorders.
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Emotional processes are crucial to the control of human behaviour and anchored to a common foundation in motivational mechanisms where emotional cues have intrinsic re-inforcement values. Emotions per se are transient events, produced in response to external or self-generated emotive stimuli, and typically characterized by attention to the stimulus, involuntary arousal reactions and changes in motor behaviour, subjective feeling states and subsequent biasing of behaviour. Primary emotions, such as happiness and fear, correspond motivationally with approach or withdrawal responses. In humans, feeling-states and subjective emotional experiences reflect cognitive contextual awareness of emotional responses and may be embellished into secondary emotions, such as guilt or relief. This review addresses the application of neuroimaging techniques to understanding the neural mechanisms supporting these aspects of emotional experience.

Normative data on cognitive measures of depression.
Dozois DJ, Covin R, Brinker JK.
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The assessment of cognition and cognitive change is important for case conceptualization, monitoring the efficacy of specific interventions, and evaluating treatment outcome in cognitive-behavioral therapy. Unfortunately, a paucity of normative data exists on cognitive measures used for psychotherapy outcome research in depression, and little information is available to guide a practitioner's understanding of the magnitude and clinical significance of a patient's cognitive change. This article presents normative data on 6 self-report instruments that assess negative and positive automatic thoughts, hopelessness, cognitive biases and errors, and dysfunctional attitudes. Normative data were derived from studies published from the date of inception of a given cognitive index to the year 2000. Recommendations for the use of these normative data are provided.
Screening for depression in medical care: Pitfalls, alternatives, and revised priorities
Steven C. Palmer*, James C. Coyne

Depression is a disorder seen commonly in general and specialty medical settings. Screening has been advocated as a means of ensuring that depressed patients are identified and receive appropriate treatment. Yet, recommendations for routine screening are frequently made without reference to empirical data demonstrating that it will have its intended effect. We examine the literature regarding screening in medical settings and suggest that screening in itself is unlikely to improve patient outcomes. Further, we identify costs to screening that are not readily apparent and that may negatively affect both patient outcomes and health-care delivery systems. We offer suggestions for how screening instruments might be used to improve the outcomes of depressed persons while minimizing negative effects on health care.

Biol Psychiatry 2003 Apr 15;53(8):640-8
Is treatment-resistant depression a unique subtype of depression?
Fagiolini A, Kupfer DJ.
Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA
Treatment-resistant depression (TRD) continues to represent a major challenge for treating clinicians. This report reviews the relevant literature to evaluate whether TRD can be considered a specific subtype of depression based on 1) clinical characteristics and course (behavioral phenotype), 2) neurobiological profile, and 3) context and environment in which TRD develops. Although patients with TRD share a number of clinical, neurobiological, and context and environment characteristics, the lack of available data and the clinical heterogeneity of this condition do not currently permit the classification of TRD as a unique subtype of depression; however, this topic is worthy of further evaluation and research. Performing genetics and neuroimaging studies on patients enrolled in large, prospective and controlled studies may provide enough data for classifying TRD (or at least a part of what is currently described as TRD) as a specific subtype of depression. This in turn may facilitate the identification of more effective treatment strategies.

J Affect Disord 2003 Apr;74(2):107-21
Evolved mechanisms in depression: the role and interaction of attachment and social rank in depression.
Sloman L, Gilbert P, Hasey G.
Leon Sloman, Centre for Addiction and Mental Health, 250 College St., Ontario, M5T 1R8, Toronto, Canada
Evolved mechanisms underpinning attachment and social rank behavior may be the basis for some forms of major depression, especially those associated with chronic stress. We note the heterogeneity of depression, but suggest that some of its core symptoms, such as behavioral withdrawal, low self-esteem and anhedonia, may have evolved in order to regulate behavior and
mood and convey sensitivity to threats and safety. Focusing on the evolved mental mechanisms for attachment and social rank helps to make sense of (1) depression's common early vulnerability factors (e.g., attachment disruptions, neglect and abuse), (2) the triggering events (e.g., loss of close relationships, being defeated and/or trapped in low socially rewarding or hostile environments), and (3) the psychological preoccupations of depressed people (e.g., sense of unlovableness, self as inferior and a failure). This focus offers clues as to how these two systems interact and on how to intervene.

Arch Women Ment Health 2003 Feb;6(1):15-22
Neurobiological effects of childhood abuse: implications for the pathophysiology of depression and anxiety.
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Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, U.S.A.

Mood and anxiety disorders are highly prevalent psychiatric disorders, especially in women, and they are associated with significant morbidity and mortality. A considerable literature indicates that vulnerability to depression and anxiety disorders is markedly increased by childhood abuse, e.g., physical, sexual, and psychological abuse, as well as adulthood stressors, e.g., death of a spouse. Little is known about the developmental neurobiological mechanisms by which childhood abuse increases the susceptibility of women to the development of depression and anxiety disorders in adulthood. Recent research on the effects of adverse early life experiences on central nervous system (CNS) stress systems has provided a greater understanding of the link between childhood abuse and susceptibility to mood and anxiety disorders. Specifically, early life traumatic events, occurring during a period of neuronal plasticity, appear to permanently render neuroendocrine stress response systems supersensitive. These physiological maladaptations likely represent long-term risk factors for the development of psychopathology after exposure to additional stress.

Stineman MG, Wechsler B, Ross R, Maislin G.
Department of Rehabilitation Medicine (Stineman, Wechsler, Ross); Leonard Davis Institute of Health Economics (Stineman); Clinical Epidemiology Unit of the Center for Clinical Epidemiology and Biostatistics (Stineman, Maislin); and Institute on Aging (Stineman), University of Pennsylvania, Philadelphia, PA.
OBJECTIVE: To apply a new tool to understand the quality of life (QOL) implications of patients' functional status. DESIGN: Results from the Features-Resource Trade-Off Game were used to form utility weights by ranking functional activities by the relative value of achieving
independence in each activity compared with all other component activities. The utility weights were combined with patients' actual levels of performance across the same activities to produce QOL-weighted functional status scores and to form "value rulers" to order activities by perceived importance. SETTING: Persons with severe disabilities living in the community and clinicians practicing in various rehabilitation disciplines. PARTICIPANTS: Two panels of 5 consumers with disabilities and 2 panels of 5 rehabilitation clinicians. INTERVENTIONS: The 4 panels played the Features Resource Trade-Off Game by using the FIMT(TM) instrument definitions. Main Outcome Measures: Utility weights for each of the 18 FIM items, QOL-weighted FIM scores, and value rulers. RESULTS: All 4 panels valued the achievement of independence in cognitive and communication activities more than independence in physical activities. Consequently, the unweighted FIM scores of patients who have severe physical disabilities but relatively intact cognitive skills will underestimate QOL, while inflating QOL in those with low levels of independence in cognition and communication but higher physical function. CONCLUSION: Independence in some activities is more valued than in others; thus, 2 people with the same numeric functional status score could experience very different QOL. QOL-weighted functional status scores translate objectively measured functional status into its subjective meaning. This new technology for measuring subjective function-related QOL has a variety of applications to clinical, educational, and research practices.

Prevalence study of signs and symptoms of temporomandibular disorders in university students.
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The aim of this study was to evaluate the prevalence of signs and symptoms of temporomandibular disorders (TMD) in university students from 19 to 25 years old, male and female, through the distribution of frequency of the data obtained from a questionnaire and physical examination. The results showed that 68% of the subjects exhibited some degree of TMD, and the women were the most affected. Signs and symptoms such as articular sounds, pain to palpation of the masticatory, cervical and scapular girdle musculature, subjective sensation of emotional stress, and postural and occlusal changes were more evident in the group with TMD, although they were also present in subjects classified as TMD-free. Limitations in the mandibular movements were not found. The association of the obtained data allowed identifying a high prevalence of signs and symptoms of TMD in the Brazilian university population.

THIS WEEK'S TOP ARTICLES

PET Study Of Methylphenidate in Adults with ADHD
Methylphenidate facilitates and disinhibits motor cortex.

Update on language disorders in autistic spectrum.

Basal Ganglia volumes in patients with tourette syndrome.

Prevalence estimations of ADHD

ADHD and brain-derived neurotrophic factor

Epileptic seizures are preceded by a decrease in synchronization.

Electroencephalography in migraine

Magnetic resonance-based techniques for MS

MRI in mental retardation.

Emotion and its disorders.

Neuropsychology of depression

Tripartite model of anxiety and depression

Neuropsychological impairment in major depressive disorder
RESPONSE BIAS

Partial cross-validation of the Wechsler Memory Scale—Revised (WMS-R) General Memory—Attention/Concentration Malingering Index in a nonlitigating sample

Archives of Clinical Neuropsychology Volume 18, Issue 1 January 2003 Pages 71-79
Robin C. Hilsabeck, a, b, Matthew D. Thompsona, c, James W. Irbya, d, Russell L. Adamsa, James G. Scotta and Wm. Drew Gouvierb

The Wechsler Memory Scale—Revised (WMS-R) malingering indices proposed by Mittenberg, Azrin, Millsaps, and Heilbronner [Psychol Assess 5 (1993) 34.] were partially cross-validated in a sample of 200 nonlitigants. Nine diagnostic categories were examined, including participants with traumatic brain injury (TBI), brain tumor, stroke/vascular, senile dementia of the Alzheimer's type (SDAT), epilepsy, depression/anxiety, medical problems, and no diagnosis. Results showed that the discriminant function using WMS-R subtests misclassified only 6.5% of the sample as malingering, with significantly higher misclassification rates of SDAT and stroke/vascular groups. The General Memory Index—Attention/ Concentration Index (GMI-ACI) difference score misclassified only 8.5% of the sample as malingering when a difference score of greater than 25 points was used as the cutoff criterion. No diagnostic group was significantly more likely to be misclassified. Results support the utility of the GMI-ACI difference score, as well as the WMS-R subtest discriminant function score, in detecting malingering.
Comparisons of two assessment measures for ADHD: the ADHD Behavior Checklist and the Integrated Visual and Auditory Continuous Performance Test (IVA CPT) were examined using undergraduates (n=44) randomly assigned to a control or a simulated malingerer condition and undergraduates with a valid diagnosis of ADHD (n=16). It was predicted that malingerers would successfully fake ADHD on the rating scale but not on the CPT for which they would overcompensate, scoring lower than all other groups. Analyses indicated that the ADHD Behavior Rating Scale was successfully faked for childhood and current symptoms. IVA CPT could not be faked on 81% of its scales. The CPT's impairment index results revealed: sensitivity 94%, specificity 91%, PPP 88%, NPP 95%. Results provide support for the inclusion of a CPT in assessment of adult ADHD.


The syndromal and subsyndromal phenomenology of borderline personality disorder was tracked over 6 years of prospective follow-up. METHOD: The psychopathology of 362 inpatients with personality disorders was assessed with the Revised Diagnostic Interview for Borderlines (DIB-R) and borderline personality disorder module of the Revised Diagnostic Interview for DSM-III-R Personality Disorders. Of these patients, 290 met DIB-R and DSM-III-R criteria for borderline personality disorder and 72 met DSM-III-R criteria for other axis II disorders (and neither criteria set for borderline personality disorder). Most of the borderline patients received multiple treatments before the index admission and during the study. Over 94% of the total surviving subjects were reassessed at 2, 4, and 6 years by interviewers blind to previously collected information. RESULTS: Of the subjects with borderline personality disorder, 34.5% met the criteria for remission at 2 years, 49.4% at 4 years, 68.6% at 6 years, and 73.5% over the entire follow-up. Only 5.9% of those with remissions experienced recurrences. None of the comparison subjects with other axis II disorders developed borderline personality disorder during follow-up. The patients with borderline personality disorder had declining rates of 24 symptom patterns but remained symptomatically distinct from the comparison subjects. Impulsive symptoms resolved the most quickly, affective symptoms were the most chronic, and cognitive and interpersonal
symptoms were intermediate. CONCLUSIONS: These results suggest that symptomatic improvement is both common and stable, even among the most disturbed borderline patients, and that the symptomatic prognosis for most, but not all, severely ill borderline patients is better than previously recognized.

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Archives of Clinical Neuropsychology
Volume 18, Issue 4, May 2003, Pages 419-429
**Measuring personality and emotional functioning in multiple sclerosis: a cautionary note**
Linda D. Nelson, Joseph T. Elder, Pany Tehrani and Jantje Groot

Changes in personality and emotional status are common in individuals with multiple sclerosis (MS). The purpose of this study was to examine results based on the MMPI-2 before and following application of a statistical correction procedure (Gass, 1992). This was done to help determine changes in scale score elevations when items containing actual physical symptoms are identified and statistically removed. Twenty-eight participants with MS were administered the MMPI-2, then retested 1 year later. Stability of MMPI-2 scores over time was demonstrated. Results showed that when the correction procedure was applied to the MMPI-2, eight standard clinical scale scores dropped an average of 6.66 T-score points. Significant differences were obtained between standard MMPI-2 scored profiles and corrected profiles on Scales 1–3 and 8. Cautious interpretation of MMPI-2 results for neurological samples was indicated. This study extended prototypic research by using patients with MS, examining the stability of results over time (1 year), and introducing a more reliable method of deriving standard T-scores in the correction procedure.

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Archives of Clinical Neuropsychology
Volume 18, Issue 4, May 2003, Pages 331-352
**A statistical analysis of board certification in Clinical Neuropsychology**
Martin L. Rohling, Paul R. Lees-Haley, Jennifer Langhinrichsen-Rohling and David J. Williamson

In this paper, we use tools from decision theory to evaluate the effectiveness of the current psychology board certification process used by the American Board of Clinical Neuropsychology (ABCN). These analyses indicate that ABCN's current process is likely to be failing to certify too many competently trained candidates, and identifying relatively few truly competent neuropsychologists. In fact, we estimate that ABCN is only certifying between 16 and 52% of competent clinical neuropsychologists. This is in contrast to the processes of the
American Board of Medical Specialties (ABMS), after which ABCN has indicated that it models its examination. ABMS estimates that 89% of all practicing physicians are board-certified by one of their member boards. Based on our analyses, specific recommendations for change are offered for credentialing the profession of neuropsychology.

This is an intriguing article about something the authors call Audio Visual Hyperactivity Disorder. 
Http://www.cmaj.ca/cgi/reprint/167/12/1331.pdf

ADD TO WEBPAGE
Add ABRP.
Add ACRM

Stroke Caregivers Handbook:

Visual Impairment Slides --> Post Listservs

Case Studies....

Susan Elmore
Mike Riley
Lisa DeBanico


The ability to detect lying was evaluated in 509 people including law-enforcement personnel, such as members of the U.S. Secret Service, Central Intelligence Agency, Federal
Bureau of Investigation, National Security Agency, Drug Enforcement Agency, California police and judges, as well as psychiatrists, college students, and working adults. A videotape showed 10 people who were either lying or telling the truth in describing their feelings. Only the Secret Service performed better than chance, and they were significantly more accurate than all of the other groups. When occupational group was disregarded, it was found that those who were accurate apparently used different behavioral clues and had different skills than those who were inaccurate.

Health Psych Div 22 Listserv subscription...
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Another Controversy:

Bigler vs Lees-Haley
On PET and Mild TBI

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Psychoneuroendocrinology
Volume 28, Issue 5 , July 2003, Pages 674-686
Impact of a unilateral brain lesion on cortisol secretion and emotional state: anterior/posterior dissociation in humans

The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum
by Eran Zaidel, Marco Iacoboni
Summarizes current research on the human corpus callosum, including animal models, normal human studies, and clinical evidence.
More info:
http://www.amazon.com/exec/obidos/ASIN/0262240440/top100
Ralph M. Reitan and Deborah Wolfson

Conation, or the ability to apply effective effort in completing a task over time, has been shown to be impaired in brain-damaged subjects. Various intelligence tests differ in the apparent extent to which they require conative ability. In this study we compared results earned by brain-damaged and control groups on three measures of intelligence: Wechsler Verbal IQ (VIQ), Wechsler Performance IQ (PIQ), and the Henmon–Nelson Test (HNT) of Mental Ability. Test scores were converted to T-score distributions for the combined groups in order to delete possible effects of differences in standardization procedures and the normative samples on which IQ scores were generated. The degree of impairment shown by the brain-damaged subjects was in direct relationship to the extent to which the three intelligence measures appear to require conation. The results support a generalization that intelligence tests that require a greater conative ability tend to produce lower scores for brain-damaged persons, as compared to controls, than do intelligence tests that are less demanding of conation.

Thomas J. Guilmette and Michael F. Paglia

Two prior surveys from rural Louisiana, Canada, and New York [Arch. Clin. Neuropsychol. 3 (1988) 331; Arch. Clin. Neuropsychol. 8 (1993) 461] revealed that a high portion of the population endorses misconceptions about the sequelae of traumatic brain injury (TBI). The purpose of this study was to assess the public's perceptions of head trauma in an urban setting in the Northeast region of the country and to compare those results with surveys from other geographical areas conducted 8 and 13 years ago. This study also examined the prevalence of perceptions about TBI that may be relevant to personal injury litigation with TBI plaintiffs. Data were collected at an office of the Department of Motor Vehicles from persons conducting business there. Participants (n=179) voluntarily completed a 19-item survey covering several facets of brain injury. This sample endorsed misconceptions at a level consistent with previous studies, indicating a comparable lack of knowledge about moderate to severe TBI. With regard to mild TBI, however, our sample generally endorsed fewer misconceptions than previous samples. The public also holds perceptions of TBI that may be relevant to personal injury litigation involving TBI plaintiffs.
Leaders of the National Academy of Neuropsychology and Division 40 (Clinical Neuropsychology) of the American Psychological Association determined that current information on the professional practice of clinical neuropsychology within the United States was needed. These two organizations co-sponsored a national survey of U.S. clinical neuropsychologists that was conducted in September 2000. The primary goal of the survey was to gather information on such topics as: practitioner and practice characteristics, economic variables (e.g., experience with major third party payors, such as Medicare and managed care), practice expenses, billing methods, experiences with Current Procedural Terminology (CPT) codes, time spent on various clinical tasks, use of assistants, and income. In this second of two articles describing the survey results, reimbursement experiences, practice economics, billing practices, and incomes are highlighted. Survey results indicate that neuropsychologists frequently have difficulty gaining access to membership on managed care panels. For those who gain access, managed care companies often limit provision of services; this is quite often perceived as negatively affecting quality of patient care. It is very common for neuropsychologists to feel obligated to provide more services to managed care and Medicare patients than are allowed to be billed to the insurance carrier; these hours are typically "written off." Numerous CPT codes are used to bill the same clinical service. Awareness of Medicare practice and billing expectations is variable among practitioners, as is awareness of public aid/Medicaid billing status. Professional income is influenced by years of licensed practice, practice setting, gender, types and amounts of non-clinical professional activities, and types and amounts of reimbursement sources within one's clinical practice. Income of neuropsychologists has only a minimal relationship to percentage of clinical practice per week. Within the context of prior surveys, neuropsychologists are engaging in more clinical hours per week and, nevertheless, compared to data from 1993, are reporting decreased income. These and other findings are presented and discussed.

Matthew M. Kurtz, J. Daniel Ragland, Paul J. Moberg and Ruben C. Gur

Studies of change in neuropsychological function over time in both healthy and diseased populations have been hindered by the absence of alternate forms of most commonly used neuropsychological tests. The Penn Conditional Exclusion Test (PCET) was developed as a new cognitive instrument to assess "executive" functioning with four alternate forms. In Study 1, the PCET was administered in counterbalanced order to 80 healthy young adults to establish equivalent test difficulty. Results revealed that the four versions were related on categories achieved, total number of errors and total number of trials. In Study 2, the PCET was administered to 25 healthy adults of a wide age range with a battery of computerized neuropsychological tests to assess construct validity. Convergent validity was confirmed by
positive correlations between the PCET and a measure of abstraction. Divergent validity was established through low, nonsignificant correlations between the PCET and measures of facial emotion recognition, word and face memory, visuospatial function, and verbal reasoning.

Frederick A. Haddad

This study provided validity evidence that the Cognitive Assessment System, Planned Codes subtest measures planning rather than speed. Each of 156 children completed Planned Codes using two different sets of directions. The first set of directions allowed each child to use strategies to complete Planned Codes. The second set of directions allowed the child only to use speed to complete Planned Codes. The results of the study indicated significantly higher scores ($t=11.5$, $P<.0001$) when the child was allowed to use strategies (mean=34.1, S.D.=9.2) compared to the same child's score when speed (mean=25.6, S.D.=7.5) alone was used to complete Planned Codes. A partial correlation, with age effects removed, between the scores each child earned under the two conditions was very low ($r=.23$; $P<.01$). Calculation of the magnitude of difference between the two groups yielded an effect size of 1.0. The results of this study provided validity support that the Cognitive Assessment System Planned Codes subtest measures planning.

John J. Randolph, Peter A. Arnett and Pamela Freske

Although previous reports have examined metamemory in various neurological groups, no study to date has examined various affective and cognitive contributors to metamemory collectively in a sample of multiple sclerosis (MS) patients. In the present study, 48 MS patients completed the Memory Functioning Questionnaire (MFQ) and were administered measures assessing depression, depressive attitudes, and executive functioning. Correlational analyses indicated that certain aspects of metamemory in MS were associated with both affective and executive variables. Structural equation modeling (SEM) analyses of three a priori models revealed the best fit with one model proposing that greater executive dysfunction and depression were associated with increased self-reported memory complaints, but via the mediating influence of depressive attitudes. Although our results suggest some objective basis for metamemory complaints in MS (i.e., executive dysfunction), they also suggest that these complaints may be exacerbated by the potentially reversible influences of depression and depressive attitudes. Treatment of depression and depressive attitudes in MS may result in MS patients having more accurate perceptions of their actual memory abilities that, in turn, may lead to improvements in their quality of life.
Concordance between the CVLT and the WMS-III word lists test, In Press, Corrected Proof, Available online 16 March 2003
Bradley D. McDowell, John D. Bayless, David J. Moser, John E. Meyers and Jane S. Paulsen

The California Verbal Learning Test (CVLT) and the Word Lists Test (WLT) from the Wechsler Memory Scale-III are widely used tests of verbal learning and memory. To examine concordance between these popular tests, we administered both to a diagnostically diverse group of 25 patients. As expected, measures from the two tests were highly correlated, although level of concordance was not as high as might be expected. When diagnostic outcomes were discordant for free recall measures, the CVLT indicated impairment more often than did the WLT.

Archives of Clinical Neuropsychology
Neuropsychological deficits among patients with late-onset minor and major depression, In Press, Corrected Proof, Available online 15 March 2003
Virginia Elderkin-Thompson, Anand Kumar, Warren B. Bilker, Jennifer J. Dunkin, Jim Mintz, Paul J. Moberg, Raquelle I. Mesholam and Ruben E. Gur

Cognitive ability of minor depressed patients (N=28), major depressed patients (N=26) and healthy elderly (N=38) was examined cross-sectionally to determine if cognitive abilities of patients with late-onset depression decrease with increasing severity of disease and if cognitive scores for minor depressed patients fall between those of healthy elderly and major depressed patients. A pooled within-group principal component analysis of cognitive test scores identified five components, three of which showed significant group differences. Verbal Recall and Maintenance of Set separated controls from major depressed patients and minor from major depressed patients. Executive Functioning separated controls from minor depressed patients, and Working Memory was borderline for separating controls from major depressed patients. The component representing Nonverbal Recognition was not statistically significant. Partial correlations controlling for age and education indicate that cognitive performance does decrease as severity of depression increases, and the magnitude of the change varies from a trend to a significant deficit depending on the cognitive domain. This decline in cognitive performance parallels a similar trend observed in neuroanatomical studies in which the volume of the frontal and temporal lobes decrease with increasing severity of depression.

Social processing deficits in agenesis of the corpus callosum: narratives from the Thematic Apperception Test, In Press, Corrected Proof, Available online 15 March 2003
Lynn K. Paul, Beatrix Schieffer and Warren S. Brown

Clinical observations suggest that individuals with agenesis of the corpus callosum (ACC) and normal IQ may have deficits in social intelligence. This study analyzed responses by normally intelligent individuals with ACC to pictures from the Thematic Apperception Test. A rating system was developed to assess three elements of story-generation: story logic, social understanding, and common content. Six individuals with ACC (five complete and one partial; IQs>85) were compared to eight controls matched for sex, age, and IQ. Based on independent rankings of story protocols by two raters, the five individuals with complete ACC were found to be significantly impaired on all three criteria. The one individual with partial ACC performed
better than the majority of controls in all three domains. Results demonstrated that individuals with complete ACC are impaired in understanding socially complex scenes and generating appropriate narratives. Absence of the anterior corpus callosum appears to be important for this deficit.


The cognitive effects of subthalamic nucleus (STN) stimulation in Parkinson's disease (PD) have been examined. However, there are no reported studies that evaluate, by incorporating a disease control group, whether neuropsychological performance in surgical patients changes beyond the variability of the assessment measures. To examine this issue, 17 PD patients were tested before and after bilateral STN stimulator implantation, both on and off stimulation. Eleven matched PD controls were administered the same repeatable neuropsychological test battery twice. Relative to changes seen in the controls, the surgery for electrode placement mildly adversely affected attention and language functions. STN stimulation, per se, had little effect on cognition. The STN DBS procedure as a whole resulted in a mild decline in delayed verbal recall and language functions. There were no surgery, stimulation, or procedure effects on depression scale scores. In contrast to these group findings, one DBS patient demonstrated significant cognitive decline following surgery.

D. Bradley Burton, Joseph J. Ryan, Bradley N. Axelrod, Tony Schellenberger and Heather M. Richards

A maximum likelihood confirmatory factor analysis (CFA) of the Wechsler Memory Scale-III (WMS-III) was performed by applying LISREL 8 to a general clinical sample (n=281). Analyses were designed to determine which of seven hypothesized oblique factor solutions could best explain memory as measured by the WMS-III. Competing latent variable models were identified in previous studies. Results in the clinical sample were crossvalidated by testing all models in the WMS-III standardization samples (combined n=1,250). Findings in both the clinical and standardization samples supported a four-factor model containing auditory memory, visual memory, working memory, and learning factors. Our analysis differed from that presented in the WMS-III manual and by other authors. We tested our models in a clinical sample and included selected word list subtests in order to test the viability of a learning dimension. Consistent with prior research, we were also unable to empirically support the viability of the immediate and delayed memory indices, despite allowing the error terms between the immediate and delayed memory subtests to correlate.
Commentary on "The lesion(s) in traumatic brain injury: implications for clinical neuropsychology", In Press, Corrected Proof, Available online 14 February 2003
Paul R. Lees-Haley, Paul Green, Martin L. Rohling, David D. Fox and Lyle M. Allen, III

Carlton S. Gass and Camille Gonzalez

The Minnesota Multiphasic Personality Inventory-2 (MMPI-2) is widely used in neuropsychology, though its length (567 items) is sometimes prohibitive. This study investigated some psychometric characteristics of the 180-item version of the MMPI-2 (Dahlstrom & Archer, 2000) in order to delineate its strengths, limitations, and appropriate scope of clinical application. Limited reliability and poor predictive accuracy were recently reported for many of the MMPI-2 short-form scales in a study that used 205 brain-injured patients. In the present investigation, we used a psychiatric sample (N=186) with normal neurological findings to examine short-form accuracy in predicting basic scale scores, profile code types, identifying high-point scales, and classifying scores as pathological (T65) or normal-range. The results suggest that, even as applied to neurologically normal individuals, the proposed short form of the MMPI-2 is unreliable for predicting clinical code types, identifying the high-point scale, or predicting the scores on most of the basic scales. In contrast, this short form can be used to predict whether the full-scale scores fall within the pathological range (T65). These findings suggest that clinicians might be able to salvage a small amount of information from the shortened (180-item) version of the MMPI-2 when MMPI-2 protocols are incomplete. However, clinicians should not use a standard interpretive approach with this test, and routine clinical application is unwarranted. Future evaluations of short-form validity should provide a more detailed examination of individual protocols, including an analysis of the frequency of accurate prediction of full-form scores.

Erin D. Bigler

The neurobiological and neuropathological bases that underlie the neuropsychological deficits associated with traumatic brain injury (TBI), including mild TBI, are further reviewed. The article provides an update on neuroimaging methods and findings in the study of TBI since the author's published address of the 1999 Distinguished Neuropsychologist Award of the National Academy of Neuropsychology (see Bigler, 2001a). The review addresses and answers criticisms raised about the interface of neuroimaging abnormalities and neuropsychological deficits, particularly in mild TBI. The article provides further guidelines in making the link between neuroimaging findings and neuropsychological outcome in the clinical practice of neuropsychology. The article also opines on the future role and importance that neuroimaging will play in neuropsychological practice, particularly functional neuroimaging method.
Patricia A. Lowe, Joan W. Mayfield and Cecil R. Reynolds

Gender differences among children and adolescents were examined on 14 separate measures of short-term memory. A nationally stratified sample of 1,279 children and adolescents, 637 males and 642 females, ranging in age between 5 and 19 years, were assessed on the 14 subtests of the Test of Memory and Learning (TOMAL). Factor structure of the TOMAL was determined to be invariant as a function of gender. Using age-corrected deviation scaled scores calculated at 1-year intervals, results of a one-way multivariate analysis of variance (MANOVA) revealed only two significant differences in absolute scores across gender on the 14 memory subtests. A profile of normal variations in patterns of memory test performance across gender revealing relative strengths for females on verbal tasks and males on spatial tasks is presented for clinical use and future normative comparisons.

The effects of motivation, coaching, and knowledge of neuropsychology on the simulated malingering of head injury, In Press, Corrected Proof, Available online 14 February 2003
Kristi Erdal

Two student groups, introductory psychology (n=91) and advanced neuroscience (n=34) undergraduates, were asked to malinger a head injury on Rey's 15-Item Test (FIT) and Dot Counting Test (DCT). The participants were randomly assigned to one of three motivation conditions (no motivation given, compensation, avoidance of blame for a motor vehicle accident) and to one of three coaching conditions (no coaching, coaching post-concussive symptoms, coaching symptoms plus warning of malingering detection). Analyses revealed a Motivation×Student Group interaction on the FIT, indicating that the advanced neuroscience students, particularly when in the compensation condition, malingered the most flagrantly. On the DCT, main effects for motivation and coaching on the qualitative variables and a Motivation×Coaching interaction on the accuracy variables indicated that those in the compensation condition performed the most poorly, and that coaching plus warning only tempers malingering on memory tasks, not timed tasks.

J. Royan, T. N. Tombaugh, L. Rees and M. Francis

A modified computer version of the PASAT (Adjusting-PSAT; Tombaugh, 1999) is described that measures speed of information processing and working memory by means of a temporal
threshold rather than number of correct responses. This is accomplished by making the duration of the interval between numbers depend on the correctness of responding—a correct response decreases the interval between digits and an incorrect response increases the interval. Modality of presentation (visual and auditory) was factorially combined with problem difficulty (answers between 2–10 or 2–18). Performance of 60 healthy student volunteers on the Adjusting-PSAT was compared to that obtained on several traditional neuropsychological measures (Digit Span, Trail Making Test, and Symbol Digit Modality Test) and on a test of basic addition skills. The visual version of the test produced a lower threshold than did the auditory version, but problem difficulty did not produce a significant effect. Of the neuropsychological tests, Trails-B (TMT-B) was most highly correlated with thresholds. However, regression analyses revealed that math ability accounted for more variance than did TMT-B. The clinical implications of these finding are discussed.

**The effect of depression and anxiety on the TOMM in community-dwelling older adults**, *In Press, Corrected Proof, Available online 14 February 2003*

Lee Ashendorf, Marios Constantinou and Robert J. McCaffrey

Tests of possible malingering are in increasing demand among neuropsychologists. The Test of Memory Malingering (TOMM) is resistant to many neurological conditions, including traumatic brain injury, dementia, and aphasia. Less clear is the impact of psychological conditions on TOMM performance. This study examined a sample of community-based older adults (55–75) to determine whether scores on the TOMM are influenced by the presence of symptoms of depression or anxiety, as measured by the Beck Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI), respectively. The results indicate that, regardless of BDI or STAI scores, all subjects scored above 45 correct out of 50 on TOMM Trial 2. These findings demonstrate that depression and anxiety levels in an older community-dwelling sample do not negatively affect performance on the TOMM.

**Normative data for elderly African Americans for the Stroop Color and Word Test**, *In Press, Corrected Proof, Available online 14 February 2003*

Robert G. Moering, John A. Schinka, James A. Mortimer and Amy Borenstein Graves

The Stroop Color and Word Test is a measure of executive function that is commonly used in neuropsychological evaluations, but for which there are currently no normative date for elderly African American individuals. The present investigation examined the influence of demographic characteristics on this measure in a community-dwelling sample of 236 elderly African American adults (60–84 years of age). Age, education, gender, and the education by gender interaction were found to affect performance on the Stroop Color and Word Test tasks. Based on these results, normative tables for Stroop Color and Word Test scores, stratified by age and with score adjustments for education and gender, are provided.
Detecting dementia with the Hopkins Verbal Learning Test and the Mini-Mental State Examination, In Press, Corrected Proof, Available online 14 February 2003
Gail Kuslansky, Mindy Katz, Joe Verghese, Charles B. Hall, Pablo Lapuerta, Gia LaRuffa and Richard B. Lipton

The Hopkins Verbal Learning Test (HVLT) and the Mini-Mental State Examination (MMSE) were administered to 323 non-demented elderly and 70 individuals who meet DSM-IV criteria for dementia in order to compare the validity of these two measures for detecting mild dementia and for the two most common dementia subtypes, Alzheimer's disease (AD) and vascular dementia (VaD). The study was conducted in an elderly, ethnically diverse community-dwelling population. Sensitivity, specificity, positive and negative predictive values were calculated over a range of clinically relevant cut scores for each test. We analyzed the influence of age, education, reading ability and sex on test performance using logistic regression models.

When sensitivity is held constant at 0.69, the specificity for the HVLT total recall was 0.89 and the MMSE 0.82 for all dementias (P=.10). Age, sex and education did not significantly influence test performance for either test in this sample. Results were similar for AD and VaD. However, while adding a measure of reading ability to the regression models did not affect the overall dementia model, it resulted in improved specificities when combined with the MMSE for AD and combined with the HVLT for VaD. Additional tests such as reading ability can improve discrimination of dementia subtypes. The modest sensitivity of either the HVLT or the MMSE alone suggests that further neuropsychological evaluation is required to confirm dementia diagnosis.

Joy H. Wymer, Katrina Rayls and Mark T. Wagner

The Wechsler Adult Intelligence Scale—Third Edition (WAIS-III) often poses problems for many populations due to the length of administration. Twenty geriatric subjects were administered the full WAIS-III. Three abbreviated forms of the WAIS-III (Satz–Mogel abbreviation (Satz & Mogel, 1962); seven-subtest short form (Ward, 1990); and a clinically derived abbreviation) were evaluated by rescoring original full WAIS-III protocols. Results showed that the abbreviated WAIS-III protocols were highly correlated with complete protocols, and classification rules were the highest for the clinically derived abbreviation. The clinically derived abbreviation was reevaluated in a college LD/ADHD population yielding similarly high correlations. Results support the use of abbreviated forms of the WAIS-III in the evaluation of elderly patients and young adults, and point to the clinically derived abbreviation as providing the smallest discrepancies from FSIQ.

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Clinical Psychology Review

**Sleep and posttraumatic stress disorder: a review**
Allison G. Harvey, , , Charlie Jones, D. Anne Schmidt

**Abstract**
Research seeking to establish the relationship between sleep and posttraumatic stress disorder (PTSD) is in its infancy. An empirically supported theory of the relationship is yet to emerge. The aims of the present paper are threefold: to summarise the literature on the prevalence and treatment of sleep disturbance characteristic of acute stress disorder (ASD) and PTSD, to critically review this literature, and to draw together the disparate theoretical perspectives that have been proposed to account for the empirical findings. After a brief overview of normal human sleep, the literature specifying the relation between sleep disturbance and PTSD is summarized. This includes studies of the prevalence of sleep disturbance and nightmares, content of nightmares, abnormalities in rapid eye movement (REM) sleep, arousal threshold during sleep, body movement during sleep, and breathing-related sleep disorders. In addition, studies of the treatment of sleep disturbance in individuals with PTSD are reviewed. **We conclude that the role of sleep in PTSD is complex, but that it is an important area for further elucidating the nature and treatment of PTSD. Areas for future research are specified. In particular, a priority is to improve the methodology of the research conducted.**

Clinical Psychology Review
Volume 23, Issue 3, May 2003, Pages 409-448

**Posttraumatic stress disorder following medical illness and treatment**
Josephine E. Tedstone and Nicholas Tarrier

Studies describing posttraumatic stress disorder (PTSD) as a result of physical illness and its treatment were reviewed. PTSD was described in studies investigating myocardial infarction (MI), cardiac surgery, haemorrhage and stroke, childbirth, miscarriage, abortion and gynaecological procedures, intensive care treatment, human immunodeficiency virus (HIV) infection, awareness under anaesthesia, and in a group of miscellaneous conditions. Cancer medicine was not included as it had been the subject of a recent review in this journal. Studies were reviewed in terms of the prevalence rates for PTSD, intrusive and avoidance symptoms, predictive and associated factors and the consequences of PTSD on healthcare utilization and
outcome. There was considerable variability both in the study methodology and design and in the results. **The highest prevalence rates were identified in patients treated in intensive care units (ICUs) and those with HIV infection. Irrespective of the physical illness, posttraumatic symptomatology is more common than PTSD caseness.** Existing characteristics of the patient may well predispose individuals to the development of PTSD as do other factors such as poor social support and negative interactions with healthcare staff. **Generally, the severity of the illness itself is not predictive of PTSD.** Issues relating to sampling, attrition, diagnosis, the course of symptoms, aetiological pathways, and the consequences of the disorder are discussed. **The presence of PTSD most probably influences the patient's use of healthcare resources and may affect their clinical outcome.**

Clinical Psychology Review  
Volume 23, Issue 3, May 2003, Pages 481-499  
**Single-session early psychological interventions following traumatic events**  
Jonathan I. Bisson  
Single-session early psychological interventions became widely advocated during the 1980s and 1990s as a way to prevent the development of psychological sequela following traumatic events. **There have now been 13 randomised controlled trials of single-session interventions within 1 month of a traumatic event.** Notwithstanding their methodological shortcomings and clinical heterogeneity, the results are neutral overall in terms of clinical effectiveness. Possible explanations include a failure to encourage individuals' personal coping mechanisms and defence mechanisms and that insufficient time was allowed for habituation to intense exposure to occur. **With the present evidence, the routine use of single-session interventions following traumatic events cannot be justified.** This does not mean that there should be nothing offered, as many individuals involved in traumatic events clearly have emotional needs. Hopefully, future research will identify alternative forms of early intervention that prove useful to those individuals who would otherwise develop more significant psychological difficulties.

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**JNCN Abstracts....**

J Neuropsychiatry Clin Neurosci 15:130-144, May 2003  
**A Critical Review of Memory Stimulation Programs in Alzheimer's Disease**  
Eric Grandmaison, M.A.Ps., L.Psych. and Martine Simard, Ph.D.  
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The authors describe the memory stimulation programs used in the treatment of Alzheimer's disease (AD) and review their efficacy. Visual imagery, errorless learning, dyadic approaches, spaced retrieval techniques, encoding specificity with cognitive support at retrieval, and external memory aids were the memory stimulation programs used alone or in combination in AD. Preliminary evidence suggests that the errorless learning, spaced retrieval, and vanishing cues
techniques and the dyadic approach, used alone or in combination, are efficacious in stimulating memory in patients with AD.

Electrophysiological Aberrations in Borderline Personality Disorder: State of the Evidence
Nashaat N. Boutros, M.D., Michael Torello, Ph.D. and Thomas H. McGlashan, M.D.
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Electrophysiological technology is noninvasive and relatively inexpensive. In order to assess the usefulness of this technology in probing the pathophysiology of borderline personality disorder (BPD), we reviewed the literature in which an electrophysiological modality was used to examine BPD. Twenty-two articles were identified, from which diagnostic criteria and data on comorbidity and control groups were extracted. Although the majority of studies pointed to a high prevalence of electrophysiological aberrations in patients, very few studies had adequate control groups and adequate evaluation of comorbidity. We conclude that although the existing literature reflects a preliminary stage of the field, it suggests that electrophysiological investigations may be useful in investigating BPD.

Clinical Correlates of Aggressive Behavior After Traumatic Brain Injury
Amane Tateno, M.D., Ricardo E. Jorge, M.D. and Robert G. Robinson, M.D. ricardo-jorge@uiowa.edu

The authors assessed aggressive behavior in 89 patients with traumatic brain injury (TBI) and 26 patients with multiple trauma but without TBI using a quantitative scale (the Overt Aggression Scale) and examined its clinical correlates. Aggressive behavior was found in 33.7% of TBI patients and 11.5% of patients without TBI during the first 6 months after injury. Aggressive behavior was significantly associated with the presence of major depression, frontal lobe lesions, poor premorbid social functioning, and a history of alcohol and substance abuse. Interventions aimed at treatment of depression and substance abuse and enhancing social support may help reduce the severity of this disruptive behavior.

Diagnostic Utility of Visual Evoked Potential Changes in Alzheimer's Disease
Kerry L. Coburn, Ph.D., James E. Arruda, Ph.D., Kristi M. Estes, M.F.T. and R. Toby Amoss, B.A. coburn_kl@mercer.edu

Previous studies have consistently found a selective delay of the P2 flash visual evoked potential (VEP) component among groups of patients with Alzheimer's dementia (AD) compared with control groups. Several authors have termed the selective P2 delay a "marker" for AD and have called for its use in clinical diagnosis. This study examined the diagnostic utility of the selective P2 delay in a retrospective sample of 45 AD patients and 60 age-equivalent healthy control subjects. Although significant between-group differences were found, classification accuracies for individual patients and controls were too low for the P2 delay to contribute meaningfully to clinical diagnosis.
The purpose of this study was to assess the cross-sectional prevalence and characteristics of anxiety among patients with Alzheimer's disease (AD), as compared with patients with frontotemporal dementia (FTD), patients with vascular dementia (VaD), and normal control subjects. The authors used the anxiety subscale of the Neuropsychiatric Inventory (NPI), an instrument with established reliability and validity, to compare patients. Patients were identified in a query of the UCLA Alzheimer's Disease Center database and included 115 patients with probable AD, 43 patients with VaD, 33 patients with FTD, and 40 normal, elderly control subjects. Descriptive statistics were generated, and partial correlations, controlling for Mini-Mental State Examination (MMSE) score, were performed between the anxiety subscale and other behavioral features as measured by the NPI and the Functional Activities Questionnaire (FAQ). Relationships between cognitive status (as indicated by MMSE score) and anxiety were explored. Anxiety was reported more commonly in patients with VaD and FTD than in patients with AD. These differences remained significant (P<0.01) in an analysis of variance (ANOVA) after adjusting for age, age at onset, educational level, and MMSE score. In AD, anxiety was inversely related to MMSE score (i.e., worse with more severe dementia), was more prevalent among patients with a younger age at onset (under age 65), and correlated with disability as measured by the FAQ score. These data suggest that anxiety is common among patients with diverse forms of dementia. In AD, anxiety is most common in those with more severe cognitive deterioration and an earlier age at onset.

Methamphetamine Dependence Is Associated With Neurocognitive Impairment in the Initial Phases of Abstinence
Ari D. Kalechstein, Ph.D., Thomas F. Newton, M.D. and Michael Green, Ph.D.

This study documented the association between neurocognitive impairment and methamphetamine dependence in a sample of 27 methamphetamine-dependent individuals who achieved 5 to 14 days of continuously monitored abstinence and in 18 control subjects. Methamphetamine-dependent individuals performed significantly worse than control subjects on neurocognitive measures sensitive to attention/psychomotor speed, on measures of verbal learning and memory, and on executive systems measures sensitive to fluency. These findings are the first to demonstrate that methamphetamine dependence is associated with impairments across a range of neurocognitive domains in a sample of users whose abstinence was continuously monitored with the use of urine screening.
Enhancement of Declarative Memory by Emotional Arousal and Visual Memory Function in Alzheimer's Disease
Hiroaki Kazui, M.D., Ph.D., Etsuro Mori, M.D., Ph.D., Mamoru Hashimoto, M.D., Ph.D. and Nobutsuguo Hirono, M.D., Ph.D
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The specific effects of visual and verbal memory on the ability of emotional arousal to enhance declarative memory were examined by using multiple linear regression analysis on data from a sample of 56 patients with probable Alzheimer's disease (AD). The enhancing effect of emotion on memory was evaluated by an illustrated story paradigm, and the visual and verbal memory by a standard memory test. In AD, memory enhancement by emotion was significantly correlated with visual memory but not with verbal memory, regardless of age, sex, educational attainment, and severity of dementia, suggesting a close association between memory enhancement by emotion and visual memory.


Effect size comparisons between analogue simulators and patients failing CARB or the WMT effort measures
Allen IL, Rohling ML, Dunn TM, Green P
Analogue experimental designs are frequently employed to validate symptom validity tests, investigate crucial aspects of test design, or explore the effectiveness of strategies intended to avoid detection of exaggeration. These paradigms typically utilize students or other normal volunteers due to the difficulty of conducting research with actual patients. It is generally assumed that these groups will closely approximate one another in Symptom Validity Test (SVT) performance. The present investigation was undertaken to test this assumption using CARB and the Word Memory Test (WMT) effort measures. Simulator data was obtained from a published study that included 100 volunteers asked to fake CARB and the WMT, who were either entirely naïve, or given up to two different strategies for defeating SVTs. The real patient (reference) group was comprised of 357 disability claimants with heterogeneous diagnoses who failed either CARB or the WMT. The entire simulator group performed far worse than real patients, producing a large effect size difference (\(d = 1.1\)). Normalized scores for simulators on CARB and the WMT were nearly identical, but real patients performed better on CARB relative to their WMT scores (\(d = 0.57\)). The results of this study raise concerns regarding the external generalizability of analogue malingering research designs.

Coping strategies moderate the relationship between cognitive dysfunction and depression in MS patients longitudinally
Arnett PA, Randolph JR, Freske PJ
Cognitive dysfunction has been shown to be inconsistently related to depression in multiple sclerosis (MS) patients. This inconsistency may be due, in part, to the influence of moderating factors heretofore unexamined. Patients with cognitive deficits commonly associated with MS may be at greatest risk for depression when they also use few adaptive coping strategies or rely differentially on maladaptive ones. The current study was designed to test this hypothesis using a longitudinal
design. The mean of z-scores from three speeded attentional measures (PASAT, Visual Elevator, Symbol Digit) and a central executive measure (Reading Span) comprised the cognitive index. The Disengagement and Active Coping indices from the COPE were used to measure maladaptive and adaptive coping, respectively, and the Chicago Multiscale Depression Inventory (CMDI) assessed depression. The COPE and cognitive tasks were administered to 49 definite or probable MS patients at Time 1, and the CMDI was administered to the same group after a 3-year interval. Regression analyses with depression as the criterion revealed significant effects for the cognitive index and active COPE index interaction \( F(1, 45) = 9.86, P < .005, r^2 = .15 \), and for the cognitive index and disengagement COPE index interaction \( F(1, 45) = 5.41, P < .05, r^2 = .09 \). Conclusions: These interactions show that disengagement and active coping both moderate the relationship between cognitive dysfunction and depression in MS. Cognitive dysfunction predicts depression longitudinally only when patients use high levels of maladaptive (disengagement) and/or low levels of adaptive (active) coping.

Abstracts / Archives of Clinical Neuropsychology 17 (2002) 719-720
Depressed MS patients recall fewer positive words than nondepressed MS patients during and after a list-learning task that suppresses subvocal repetition
Bruce J, Arnett P, Strober L, Polen D, Smith M
Forty to sixty percent of multiple sclerosis (MS) patients have observable memory deficits and approximately 50% experience clinical or subclinical depression. Nonetheless, relatively little is known about how depression may affect memory disturbances in MS. Previous research in non-MS depressives has demonstrated a direct relationship between depression and difficulty remembering positively laden material. One hypothesis is that “positive neglect” occurs because depressed patients employ less subvocal repetition when they are presented with positively laden words. In the current investigation, depressed \( (n = 21) \) and nondepressed \( (n = 30) \) MS patients attempted to recall positive and negative words that were presented as part of a working memory task that prevented subvocal repetition. Depressed MS patients recalled significantly fewer positively laden words than nondepressed patients during the task and at a delay (both \( P < .05 \)). During the task, nondepressed MS patients recalled a higher percentage of positive words (53%) than depressed MS patients (50%, \( P < .05 \)). At the delay, 55% of the words recalled by nondepressed patients were positively valenced compared with 40% of the words recalled by nondepressed patients (\( P < .05 \)). A statistical trend was also noted in which depressed patients retained fewer positive words than nondepressed patients (\( P = .06 \)). In this study, the suppression of subvocal repetition did not negate positive neglect in depressed MS patients.

Abstracts / Archives of Clinical Neuropsychology 17 (2002) 729
Collateral rating of memory impairment: misappraisal due to depression
Patton DE, Duff K, Schoenberg MR, Scott JG, Adams RL
The present study sought to determine the extent to which patients’ emotional factors influence howthey are perceived cognitively by collateral informants. It was hypothesized that emotional factors, such as depression, would lead a patient to be viewed as functioning below their actual ability level. To test this hypothesis, a mixed clinical sample of 95 patients ages 57–79 (mean = 69.6, S.D. = 5.66) referred for neuropsychological assessment were divided into two groups based on the difference z-score (z-DIFF) between their actual memory (i.e., z-score on RAVLT Trial 7) and a collateral’s appraisal of their memory (i.e., z-score on the CBRS MD scale). Patients in the OVEREST \( (n = 26) \) group had z-DIFF scores = +1.0, suggesting that collaterals underestimated their abilities. The groups were compared on the Geriatric Depression Scale (GDS). The UNDERST group scored significantly higher than the OVEREST group on the GDS. The two groups did not differ significantly on age or DRS Total Score. Depressed patients were perceived by collaterals as functioning below par with regard to memory, despite the fact that their actual performance suggested that their functioning was intact. Conversely, nondepressed patients were viewed as functioning within normal limits by collateral informants, despite the fact that their actual performance suggested that their functioning was impaired. These findings suggest the need to consider potential moderating factors when interpreting collateral ratings of patient
The effects of depression on neuropsychological test performance
Brown LJ, Letsch EJ, Vanderploeg RJ

Despite extensive research investigating the impact of depression on cognitive functioning, controversy remains as to whether depression results in deficits in specific cognitive domains or impairment in global performance. This study examined the neuropsychological test performance of depressed Vietnam era veterans to ascertain the extent and the nature of cognitive impairment within this group. The current studies utilized a nonreferred, community-dwelling sample of 4,462 male veterans who received medical, psychological and neuropsychological evaluations as part of the Vietnam experience study. Language, visual and verbal memory, visual–spatial and constructional abilities, attention, speed and coordination, and executive functioning were assessed. IQ was measured at military enlistment and for the study. MANOVAs assessed the relationship of depression to cognitive performance in two samples utilizing different inclusion criteria for depression compared to demographically matched control groups. Participants with depression, as measured by MMPI Scale 2 elevations over T-scores of 70 (n = 97), demonstrated deficits on tests of attention, memory, and verbal fluency compared to a control group without MMPI elevations (n = 200). There was no difference in the cognitive performance of participants with depression, as determined by DSM-III diagnostic criteria paired with elevations on at least Scale 2 (n = 136) compared to a control group without a diagnosis of depression (n = 197). In both studies the interaction between time and depression was significant in that the depressed groups’ IQ declined on repeat testing compared to controls. Depression affects performance in specific cognitive domains as well as intellectual functioning over time. Potential reasons for the different findings in the two studies are discussed.

The effect of anxiety and depression on neuropsychological functioning 810
Schoenberg MR, Duff K, Adams RL, Beatty WW, Scott JG

While the impact of depression on neuropsychological functioning has received considerable research attention, the role of anxiety on neuropsychological functioning has received less interest (but see Beatty et al., in press; Gibbs et al., 1991; Kizilbash et al., 2001; Ryder et al., 2001; Unkenstein & Bowden, 1991; Wiens et al., 1988). The present study investigated the effects of anxiety and depression on neuropsychological functioning in a mixed clinical sample of 157 patients. Participants were categorized into four groups (high anxiety/high depression, high anxiety/low depression, low anxiety/high depression, and low anxiety/low depression) based on their scores on self-report anxiety (STAI) and depression (BDI) tests. Subjects were compared on measures of attention (Trials A, WAIS-R Arithmetic and Digit Span subtests, WMS-R Attention/Concentration Index), memory (RAVLT 30-min delay, WMS-R General Memory and Delayed Memory indices), and sequencing/mental flexibility (Trials B, COWAT). Results yielded no significant main effects for anxiety or depression on neuropsychological functioning but there was a significant interaction effect (P < .05) for anxiety with depression in which high anxiety adversely affected attention (Trials B, COWAT) performances when patients’ self-reported high levels of depression. Given the negative effects of anxiety on attention and mental flexibility, clinicians are advised to routinely assess and consider anxiety when interpreting test performances.

Does TEST ANXIETY impede neuropsychological test performance?
Gass CS

Experimental research findings suggest that many individuals perform more poorly on tests because they exaggerate and personalize inordinately the threat of evaluation. Relevant research in neuropsychology has focused on psychopathology without regard to the specific impact of the testing context. The present study used the Test Anxiety Profile (TAP; Oetting & Deffenbacher, 1980) in a format adapted specifically to the neuropsychological testing context. A sample of 253 male neuropsychological referrals (average age = 52.5, education = 11.9, FSIQ = 95.9) were administered the modified 12-item TAP immediately following completion of an expanded Halstead–Reitan neuropsychological test battery. These examinees were judged to be neurologically intact by staff neurologists independent of neuropsychological test results. The sample’s diagnostic composition included depression (43%), generalized anxiety (20%), and PTSD (17%). Test anxiety scores were significantly related to average impairment rating (r = .304), WAIS-R Full-Scale IQ (r = .351), and WMS-R Logical Memory-II scores.
(r = .32, all P < .001), but not to scores on the WRAT-R Reading (r = .049, n.s.). TAP scores were also related to scores on MMPI-2 Scale 7 (r = .456, P < .001). Examinees were classified as high- versus low-test anxious based on TAP scores. Mean scores in the high-test anxious group were significantly poorer on eight out of nine performance measures. These results are consistent with a hypothesized impact of anxiety on test performance. However, they do not demonstrate a causal direction. Further research is warranted.

An examination of the relationship between MMPI Depression Scale and performance on the Halstead–Reitan Test Battery

Pospisil T, Kirsten A, Chuplis KA, Conger C, Golden CJ

Given the prevalence of the administration of both the MMPI-2 and various tests from the Halstead–Reitan Neuropsychological Test Battery, it is important to recognize patterns of performance while interpreting the results. The purpose of the following study was to examine the relationships between the Depression Scale from the MMPI-2 and selected tests from the Halstead–Reitan Test Battery. Participants were 155 adults referred for a full neuropsychological evaluation assessing for possible psychiatric and/or neurological disorders. The average age of the participants was 37.71 (S.D. = 15.44), they completed on average 13.12 years of education (S.D. = 2.91), 57.4% were female, and the majority of them were right-handed (87.7%). The sample was predominantly Caucasian (72.9%), with 13.5% African-American and 9.7% Hispanic. Pearson’s product correlations were performed between Scale 2 from the MMPI-2 and The Finger Tapping Test, Trails A and B, Tactual Performance Test (TPT), and the Category Test. Significant correlations (a = .05) were found between the Depression Scale and The Finger Tapping Test (Dominant, r = .244; and Nondominant, r = .242), Trails A (r = .256), Trails B (r = .327), and the TPT Both Hands (r = .222). The apparent psychomotor retardation present in patients endorsing items from the Depression Scale needs to be recognized while interpreting poor performance on neuropsychological measures. While the relationships are mild, they can influence results especially when client’s performance are near “cutoff” scores. These results highlight the importance of identifying the relationship between personality and neuropsychological performance while interpreting test results.

Abstracts / Archives of Clinical Neuropsychology 17 (2002) 773

Impact of pain on postconcussive symptoms

Smith-Seemiller LH, Fow NR, Kant R, Franzen MD

The etiology of postconcussive syndrome (PCS) has been debated, with research suggesting that PCS symptoms are not unique to people with closed head injury (CHI). In previous research we compared people with chronic pain (CP) to people with CHI on a measure of PCS and found similarities between these groups. In this study, we sought to further explore the relationship between pain and PCS symptom ratings by (1) comparing people with both CP and CHI to patients with only one diagnosis and (2) studying the relationship between pain ratings, depression, and PCS ratings. Subjects included 67 CP patients with no history of neurological problems, 55 CHI patients, and 38 patients with CHI and a separate CP problem. Patients completed the Rivermead Postconcussion Questionnaire (RPCQ). Differences in summary scores between the three groups were analyzed using Kruskal–Wallis ANOVA by ranks, correlations between RPCQ scores and pain ratings were computed, and regression equations were used to study the relationship between pain ratings and PCS symptoms after controlling for litigation status and BDI scores. People with both CP and CHI had higher total scores on the RPCQ than either of the other groups. Pain ratings were significantly correlated with total RPCQ scores, even with the effects of litigation and depression controlled. However, pain ratings were correlated only with somatic and emotional symptoms of PCS, and not with cognitive complaints. It is concluded that CP is a significant but often over-looked factor in the maintenance of PCS symptoms.

Review and meta-analysis of neuropsychological findings in PTSD

Dearth CM, Rinaldo JC, Berry DT, Schmitt FA
We present a comprehensive review of neuropsychological findings in PTSD data published in peer-reviewed psychological and medical journals. Data published since 1989 suggest that persons with PTSD demonstrate average intellectual abilities, verbal comprehension and reasoning, and visual–spatial performance. Relative to control samples, persons with PTSD frequently display decreased working memory, complex attention processes, olfactory discrimination, verbal learning, and memory. Although these performances are lower than controls, persons with PTSD typically perform within the average range for these cognitive areas. Meta-analysis of neuropsychological performances among PTSD and control participants in combat veteran samples reveals small to medium effect sizes for PTSD symptoms on cognitive functioning, with largest effect sizes obtained for working memory and verbal memory tasks. As most neuropsychological studies of PTSD focus on combat or POW samples, it is unclear whether relative deficits generalize to other PTSD populations, such as sexual abuse survivors. In many cases, failure to exclude patients with previous neurological injury and previous or current substance use confounds inferences of decreased cognitive functioning based on PTSD symptoms alone. Additionally, few studies administer a test of effort/motivation as an exclusion criterion, despite the possibility of poor motivation in clinical referral streams.

Quantitative electroencephalographic assessment of an individual with comorbid depression and panic attacks
Foster PS, Harrison DW
Considerable research has indicated that anxiety is often associated with dysfunction within the frontal lobes. However, inconsistencies have emerged concerning whether the cerebral dysfunction is characterized by increased left frontal or right frontal activation. Whereas some have found increased left frontal lobe activation with anxiety (Tucker, 1981), others have reported that anxiety is associated with increased right hemisphere activation (Reiman et al., 1984) and lesions within the left frontal lobe (Heilman & Valenstein, 1993). Heller (1993) has proposed that different patterns of cerebral activation may be associated with anxiety characterized by panic as opposed to excessive worry. Specifically, in contrast to excessive worry, anxiety characterized by panic may be associated with increased right hemisphere activation. The present research presents the case of a 20-year-old, right-handed, female who was referred for a neuropsychological evaluation due to experiencing depression and recurrent episodes of panic attacks that occasionally result in loss of consciousness. The results of standardized testing and syndrome analysis led to the a priori hypothesis of left frontal lobe dysfunction. This a priori hypothesis was subsequently tested using quantitative electroencephalography (QEEG). The results of the QEEG confirmed the a priori hypothesis in that decreased magnitude values across all bandwidths measured (high delta, theta, alpha, beta) were noted in the left frontal and central regions, as compared to the homologous regions. Thus, the present findings support the hypothesis of increased right hemisphere activity and left frontal lobe dysfunction in individuals with anxiety disorders.

Verbal learning and memory in pediatric bipolar disorder 809-810
Giuliano AJ, Garroway J, Stein N, DeJong S, Beiderman J, Frazier J
Despite the morbidity associated with bipolar disorder (BPD), few studies have investigated the nature of cognitive impairment in BPD. The purpose of this study was to contribute to an emerging understanding of cognition in pediatric BPD. The CVLT-C performance of 59 children (37 bipolar; 22 control) with a mean age of 10.62 (S.D. = 2.89) was compared. The groups were statistically equivalent in age and education; however, the control group had a significantly higher WISC-III verbal IQ and freedom from Distractibility Index (FDI). Significant findings using ANCOVA, with VIQ as the covariate, revealed that the groups performed comparably on the first learning trial, but the BPD group showed reduced total learning, recall consistency, List B recall, and semantic learning strategies (P < .01). Trends suggested that BPD children produced more perseverative responses and intrusions (P <.10). Savings score rates between groups were statistically equivalent. Findings were comparable when FDI was used as a covariate and when gender was included in a factorial ANCOVA. The BPD group’s total learning score was one-half S.D. below the score for the age-appropriate normative group (mean = 45.18, S.D. = 13.03). These findings suggest that pediatric BPD is associated with verbal learning and memory deficits, and the pattern of deficits appears, in large part, due to executive dysfunction (i.e., deficits in organizational/strategic encoding, working memory, sustaining a learning and retrieval plan,
An examination of executive function in major depressive disorder—a role in recovery?
Withall A, Harris L, Cumming S

We attempted to delineate the executive functions affected by major depressive disorder. One of the criteria for a depressive episode is a diminished ability to think or concentrate, or indecisiveness, nearly every day (DSM-IV, 1994). Patients report these symptoms as frustrating and disheartening and evidence suggests their problems persist postdischarge, making a successful return to employment difficult. Executive function is important for daily life and both neuropsychological and neuroimaging studies support deficits in depression. Previous studies however have not extensively tested the individual domains of executive function affected in depressed patients. A comprehensive psychiatric (HRSD-21, Depression Anxiety Stress Scale, Frontal Lobe Personality Scale) and neuropsychological assessment (NART, reaction time, digit span, CVLT, COWAT, WCST, Stroop, WISC-III mazes, prospective and source memory, six elements test) was administered at admission, discharge and 3-month follow-up to patients and age, sex and IQ-matched controls. Thirty-five patients were recruited from The Royal North Shore Hospital and Northside Clinic, Australia, aged 20–60 years, and with a primary diagnosis of major depressive disorder. Preliminary analyses show patients perform similarly to controls on structured tests, however the six elements test which requires patients to organize, monitor and review their performance shows significant deficits associated with depression. These deficits remain present at follow-up, as do significant levels of depressive symptoms. **We conclude that it is necessary to monitor patients’ recovery on a long-term basis since depression may not remit and persistent executive deficits may be the best predictor of the ability to return to work for depressed patients.**

Abstracts / Archives of Clinical Neuropsychology 17 (2002) 822-823

How common is malingering in litigated cases?
Hartlage LC, Johnson DJ

The issue of malingering in neuropsychological assessment involving litigated cases represents an area of controversy and importance. Estimates of malingering—using diverse criteria—have ranged from below 10% to greater than 50%. Often, ‘malingers’ have been individuals instructed to feign neuropsychological impairments rather than individuals empirically demonstrated to be malingering in a natural setting, so that such studies do not clarify incidence questions. **This study compared 42 individuals referred for neuropsychological assessment who were actively involved in litigation with alleged traumatic brain injury (i.e., high malingering risk, with focus on impairments); with a matched group of individuals seeking vocational rehabilitation assistance to pursue schooling (i.e., low malingering risk, with focus on educational potential) who had been referred for neuropsychological assessment of CNS functional status. Comparisons of *t*-tests on MMPI 2 validity scales and *F* . *K* ratio; Rey 16-Item Test; and HRNB scales demonstrated sensitive to malingering were computed, for total of seven *t*-tests. There were no differences (*P* < .05) on any of these seven tests, although the two groups did differ on other measures (i.e., Depression, Impairment Index) not necessarily indicative or suggestive of malingering. There was good congruence among measures of malingering and clinical estimates of malingering on qualitative basis. **Findings suggest incidence of malingering in litigated cases may be lower than many estimates.**

Wechsler Memory Scale-III Faces subtest performance in head injured and probable malingering patients
Mittenberg W, Zieman SF, Legler W, Patton C, Azrin R

Forced choice recognition memory tests are often useful in the identification of insufficient effort or symptom exaggeration. These measures are typically evaluated to determine if scores are lower than those obtained by patients with cognitive impairment or if scores are less than would be obtained by chance. **This study compared the WMS-III Faces subtest performances of 48 nonlitigating head injured patients to that of 25 probable malingers to determine the diagnostic utility of various cut-off**
scores. Patients were examined an average of 9.5 months after mild ($n = 15$) or moderate ($n = 33$) head trauma. Litigants scored below probable malingering cutoffs on the TOMM or portland digit recognition an average of 24 months after minor or mild head trauma. Probable malingerers obtained significantly lower scores on the Faces subtests than head injured patients. No head injured patient scored below 24/48 on Faces 2 or 49/96 on the total of the Faces 1 and 2 trials. 20% of probable malingerers performed below these cut-off scores. 95% of head injured patients scored above 26/48 on the Faces 1, 28/48 on Faces 2, and 56/96 on the total of the Faces trials. Twenty-four percent of probable malingerers performed below one or more of these cut-off scores. Application of the binomial theorem to the faces subtests indicates that scores of 18 or less on Faces 1 or 2 and 39 or less on Faces total fall significantly below chance at the .05 level. Eight percent of probable malingerers scored significantly below chance on one or more of these measures.

Comparing litigants suspected of malingering and simulators on the Memory Assessment Scales
O'Bryant SE, Duff K, Fisher JM, McCaffrey RJ
A common practice in research examining symptom exaggeration/malingering is the use of simulators. In these research paradigms, participants, typically undergraduate students, are asked to feign symptoms associated with brain injury. Although there is considerable question as to the generalizability of these research findings, few investigations have explicitly compared simulators to TBI patients suspected of malingering. The purpose of the present study was to compare litigants suspected of malingering to simulators on the Memory Assessment Scales. The litigants suspected of malingering (based on TOMM and/or Rey-15 performance) consisted of 29 mild TBI patients referred to a private neuropsychological practice due to MVA or work-related accidents. The scores obtained by the litigant groups were compared to those obtained by the simulator group utilized in Beetar and Williams (1995). Multiple, Bonferroni-corrected $t$-tests were computed, and the simulator group scored significantly higher than the litigants suspected of malingering on all 4 of the MAS Summary Scores and 8 of the 12 subtest scores. The present results indicate that simulators may provide an underestimation of how suspected real life malingerers may perform on the Memory Assessment Scales and shed further doubt on the utility of simulator research.

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Abstracts / Archives of Clinical Neuropsychology 17 (2002) 865
The influence of legal referral source on performance of the Test of Memory Malingering (TOMM) in adults with traumatic brain injury
Stott HD, Black FW
Effort and motivation have been important factors in neuropsychological test performance. The importance of detecting malingering is particularly important within patients involved in litigation cases. The impact of various neurological conditions and emotional conditions have been investigated using the Test of Memory Malingering (TOMM), although the effect of referral source on test performance within litigating cases has not been examined. The present study investigated 115 participants (62 defense; 53 plaintiff) with closed head injury referred for comprehensive neuropsychological evaluation. A one-way ANOVA on the participants indicated that plaintiff referrals showed significantly higher scores on all three trials of the TOMM. These results demonstrate that individuals with a legal referral source of plaintiff performed significantly better on the TOMM than those with a referral source of defendant, suggesting the importance of legal referral source as an additional factor in measures of effort and malingering. Implications and ideas for future research are discussed.

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Poster twins: a profile of two malingerers 865
Wymer J, Gouvier WD
Although testing observations and objective measures are commonly used to identify probable malingerers, rarely do neuropsychologists receive absolute confirmation that their probable diagnoses are correct (as malingerers are not likely to admit their impression management). Two brain injured patients, one mild and one severe, were evaluated in a medicolegal context to determine the effects of their brain injuries, strengths, and residual deficits. Both patients were identified as malingering with the use of forced choice tests (Warrington Recognition Memory Test (RMT), Test of Memory Malingering
(TOMM), and Word Memory Test (WMT)), easy measures designed to have high face valid difficulty (Memory for 15-Item Test (MFIT) and WMT), aberrant intrasubtest scatter, and discrepancy between identified injuries and test findings. Both patients received a session of values clarification by their attorney designed to engender more honest and full participation. The severely head injured patient confessed to exaggerating her deficits, while the mildly injured patient denied exaggeration. Both patients are scheduled to be reevaluated using some parallel and some identical measures, and their pre–post profiles will be discussed in light of their recanting versus not.

Intelligence and successful malingering on forced-choice tests: an initial investigation 859
Carruth D, Perkins S, Crosby J, Andrade I
Malingering is reported to be common in forensic and compensation-seeking samples, with estimates of faked or exaggerated symptomatology ranging from 14.5 to 60%. Findings have also indicated that subjects are capable of producing response profiles on standard batteries which are not routinely detected by clinicians. This dilemma has led to increased efforts to identify patterns which suggest malingering and develop specific procedures which indicate malingering. Forced-choice tests are believed to accurately indicate malingering by comparing correct response rates to chance or predetermined levels based on normative and patient samples. This study investigated the subject’s intellectual ability and sophistication in simulating believable cognitive deficits. Undergraduate student participants completed the WASI and a forced-choice task and correlations between intelligence and presented cognitive deficit levels were compared and a significant relationship was observed between Full-Scale IQ and the number of correctly-answered trials ($r = .326; P < .043$). Dichotomous analysis of groups means (correct trials) between groups of subjects classified as high or low in intellectual ability were also calculated for clinical utility and those classified as high intelligence showed a significantly higher mean of correctly-answers than did low subjects [$F(1, 24) = 5.553; P < .027$]. Analyses of mean scores for each group were also compared to chance performance rates and high intelligence participants were found to more often pass detection at this level [$z = 4.887, P < .027$]. The clinical relevance of the findings are discussed in addition to limitations of this study and directions for future research.

Longitudinal predictors of learned helplessness in MS
Polen DM, Arnett PA
Individuals with multiple sclerosis (MS) consistently show high rates of depression. Shneker et al. (1995) found that a measure of learned helplessness predicted depression better than other attributional measures in these patients. Interestingly, learned helplessness has long been theorized to be a final common pathway to depression generally. The present study was designed to explore whether three core features of MS–MS disability, fatigue, and cognitive dysfunction—predict learned helplessness longitudinally. Method: Fatigue (Fatigue Impact Scale, FIS), cognitive function (mean z-score of Tower of London indices, visual elevator subtest from the test of everyday attention, symbol digit, PASAT, and reading span), and MS disability (EDSS) were assessed 3 years prior to the measure of learned helplessness (MS Attitudes Index, MSAI) in 49 definite MS patients. Correlational analyses revealed that the MSAI correlated significantly with FIS ($r = .37, P < .01$), cognitive function ($r = .35, P < .01$), and EDSS ($r = .46, P < .001$) measures. Stepwise regression analysis indicated that both the EDSS and the FIS contributed significant ($P < .002$ and $P < .05$, respectively) unique variance to scores on the MSAI ($r^2$ change values $= .21$ and .07, respectively). Our results suggest that at least two factors—MS disability and fatigue—may independently affect the development of learned helplessness in MS patients, something that is likely to put these individuals at risk for depression. Psychotherapeutic treatment that targets perceptions of learned helplessness may reduce this risk.

Coping and hoping: two possible buffers against general psychopathology in MS patients
Schurle AC, Arnett PA
Although depression has been studied extensively in multiple sclerosis (MS) patients, little attention has been devoted to exploring possible contributors to and buffers for psychopathology more generally. In
the current study, we examined whether two variables shown to serve as protective factors for depression in other patient groups—optimism and active coping—would be inversely related to generalized psychopathology in MS patients. Method: The following measures were included: an Active Coping Index created from several subscales of Carver et al.'s (1989)COPE measure, thought to measure adaptive coping; the agency component of the Hope Scale assessing an individual’s general optimism; and the Global Severity Index (GSI) of the SCL-90-R, assessing current level/depth of generalized psychopathology. Procedure: Measures were administered to 46 definite MS patients. Results: Strong negative correlations were found between both the Active Coping Index ($r = .46, P < .002$) and the Hope-Agency Index ($r = .49, P < .002$) with the GSI. Hierarchical regression analysis revealed that the Active Coping Index accounted for 21% ($P < .002$) of the variance in the GSI and the Hope-Agency Index accounted for an additional 9% ($P < .05$). Conclusions: Both active coping and optimism are inversely related to generalized psychopathology in MS patients. These factors may serve as buffers for the development of psychopathology in these patients. Because it has been demonstrated that coping strategies and an individual’s level of optimism can be modified through cognitive behavioral psychotherapy, targeting these factors in MS patients may help reduce their generalized psychopathology.

**Disease severity, sleep disturbance, and depression as predictors of fatigue in MS: a longitudinal study**

*Strober LB, Arnett PA, Bruce JM, Polen DM, Smith MM*

Fatigue in multiple sclerosis (MS) is a common and debilitating problem. Despite its high prevalence, the etiology of fatigue is still poorly understood. In the present study, we looked at several possible predictors of fatigue longitudinally: disease severity, depression, and sleep disturbance. We studied 52 definite MS patients (mean age = 46.4; EDSS = 4.5; education = 15) at Time 1 and then at Time 2, 3 years later. Stepwise regression analysis showed that sleep disturbance at Time 1 ($R^2 = .23; P < .001$) was the best predictor of fatigue at Time 2, followed by disease severity ($D R^2 = .13; P < .005$) and lastly, depression ($D R^2 = .07; P < .05$). These results suggest that sleep problems, disease progression, and depression may serve as risk factors for fatigue in MS. As such, treatment of these factors may result in a reduction of patients’ fatigue and subsequent improvement in their quality of life.

**The effect of APOE on unawareness of cognitive deficit and depression in Alzheimer’s disease**

*Wagner M, Bachman D*

The objective of this study was to test whether the APOE gene influences the expression of unawareness of cognitive deficit in Alzheimer’s disease. The punitive APOE four allele has been shown to increase the risk of Alzheimer’s disease and is associated with earlier onset. It is less clear whether the punitive four allele influences the behavioral expression. The sample consisted of 57 sequential patients seen for diagnostic evaluation who met NINCDS/ADRDA criteria for probable Alzheimer and who fell within the CDR questionable or mild dementia severity range. Standard diagnostic procedures were followed. APOE was assayed and unawareness was determined using a measure with sound properties of reliability and validity. Patients were grouped according to the presence of the four allele, with the APOE 2:3 and 3:3 combined (absent, $N = 16$), and the APOE 3:4 and 4:4 combined (present, $N = 41$). Data were analyzed using a 2 x 2 ANOVA with APOE and CDR as the independent variables and unawareness of cognitive deficit or depression as the dependent variables. For unawareness, there were significant main effects for APOE ($P < .0001$) and CDR ($P < .0065$), but no interaction. For depression, there was a main effect for APOE status ($P < .019$), but not dementia severity, with no interaction. It was concluded that independent of dementia severity, those with the punitive APOE four allele had greater awareness of cognitive deficit and more Depression.
An investigation of the relationship between personality traits and executive functioning
Tsanadis J, Suhr JA
While personality and cognitive changes associated with frontal lobe damage (i.e., executive functioning) have been well documented, there has been little research on the association of executive functioning to normal variation in personality traits. Many of the traits measured by personality tests (i.e., tough mindedness, self-control) describe qualities consistent with those measured by tests of executive functioning. In this study, 142 undergraduates completed the Sixteen Personality Factor Questionnaire (five global factors), the Wisconsin Card Sorting Test (WCST), the Wechsler Abbreviated Scale of Intelligence (WASI), and Bechara’s Gambling Task. Principal component factor analysis with varimax rotation revealed four factors. The first factor, consisting of executive functioning measures, validates the gambling task as a measure of executive functioning. The second factor consisted of loss of set (WCST), gambling task, and VIQ and PIQ. This indicates the expected relationship between intelligence and executive functioning in the normal population. The third factor consisted of the personality traits tough mindedness, self-control, and loss of set (WCST) and VIQ, suggesting a relationship between personality traits related to a person’s openness to new things and ability to restrain themselves with aspects of executive functioning involving a person’s ability to maintain a mental set. The fourth factor is made up of several personality traits (extraversion, anxiety, independence, self-control), as well as VIQ and gambling task. These findings support the relation of cognitive measures of executive functioning and normal variations in behavior that are part of personality differences.

Neuropsychological predictors of nonepileptic seizures
Wagner M, Pritchard P, Topping K
Neuropsychological testing has been used to aid in the diagnosis of epileptic (ES) versus nonepileptic seizures (NES). In addition to neurocognitive screening, we believe that this data is the first time the PAI has been assessed relative to the NES/ES differential. Eighteen consecutive patients who completed long-term video EEG monitoring were diagnosed with either NES and nine had ES. The mean age was 35.4. There were no significant cognitive group differences. On the PAI, T-test group comparisons with showed no group difference on any of the validity scales. Group differences were found on the depression ($P < .032$), treatment rejection ($P < .029$), and dominance ($P < .043$) scales. The subscale conversion disorder showed large group differences ($P < .010$). The NES group had greater physiologic signs of depression, were more willing to endorse the need for personal psychological change, and were retiring in personality style. Most striking difference was the NES group’s tendency to endorse functional impairment due to symptoms associated with sensory and/or motor deficits (conversion). Using the conversion subscale scale only, a sensitivity of 67% and a specificity of 89% were found in classifying seizure type. While neurocognitive variables did not reveal group differences, the PAI shows promise in aiding in the differential diagnosis of NES versus ES and may prove useful in the development of psychiatric treatment planning for NES patients.

Impact of pain on postconcussive symptoms 772-773
Smith-Seemiller LH, Fow NR, Kant R, Franzen MD
The etiology of postconcussive syndrome (PCS) has been debated, with research suggesting that PCS symptoms are not unique to people with closed head injury (CHI). In previous research we compared people with chronic pain (CP) to people with CHI on a measure of PCS and found similarities between these groups. In this study, we sought to further explore the relationship between pain and PCS symptom ratings by (1) comparing people with both CP and CHI to patients with only one diagnosis and (2) studying the relationship between pain ratings, depression, and PCS ratings.
Subjects included 67 CP patients with no history of neurological problems, 55 CHI patients, and 38 patients with CHI and a separate CP problem. Patients completed the Rivermeade Postconcussion Questionnaire (RPCQ). Differences in summary scores between the three groups were analyzed using Kruskal–Wallis ANOVA by ranks, correlations between RPCQ scores and pain ratings were computed, and regression equations were used to study the relationship between pain ratings and PCS symptoms after controlling for litigation status and BDI scores. People with both CP and CHI had higher total scores on the RPCQ than either of the other groups. Pain ratings were significantly correlated with total RPCQ scores, even with the effects of litigation and depression controlled. However, pain ratings were correlated only with somatic and emotional symptoms of PCS, and not with cognitive complaints. It is concluded that CP is a significant but often over-looked factor in the maintenance of PCS symptoms.

Mild TBI

*Archives of Clinical Neuropsychology 17 (2002) 767-768*

**The relationship between daily stress and persistent postconcussion symptoms following a mild traumatic brain injury**

*Ford SM, Swirsky-Sacchetti T, Chute D*

The purpose of the present study was to determine the extent to which daily stress predisposes a clinical population of mild TBI patients diagnosed with postconcussion syndrome (PCS) to postconcussive symptoms. Eight individuals diagnosed with PCS and eight nonbrain-injured individuals were matched for age, education, IQ, and race. Daily stress levels and postconcussion symptoms were tracked over a 4-week period using the Postconcussion Symptom Checklist and the Daily Stress Inventory. Measuring symptoms and daily stress over time increased the likelihood of assessing symptoms during low- and high-stress days. Results from the ANOVAs indicated that the PCS group endorsed greater frequency \( F(1, 14) = 19.10, P = .001 \); intensity \( F(1, 14) = 28.90, P < .001 \); and duration \( F(1, 14) = 33.79, P < .001 \) of symptoms compared to the nonbrain-injured group. Under high stress conditions, the PCS group reported a greater relative increase in the frequency \( F(1, 14) = 11.74, P = .004 \) and the intensity \( F(1, 14) = 6.96, P = .02 \) of symptoms compared to the nonbrain-injured group. When perceived stress was the independent variable, a significant repeated measures effect was revealed for the frequency \( F(1, 14) = 21.23, P < .001 \); intensity \( F(1, 14) = 39.50, P < .001 \); and duration \( F(1, 14) = 26.49, P < .001 \) of symptoms in the PCS group. These findings suggest that individuals with PCS are more susceptible to the effects of daily stress than nonbrain-injured individuals and that stress reduction interventions may be beneficial in managing postconcussive symptoms.

**Increased risk for concussion in female athletes**

*Hillary FG, Mann, C, Schatz P*

The incidence of sports-related concussion in high school and college athletes is high, with 34–97% of athletes reporting one or more previous concussion. Despite the growing sports-concussion literature, there has been greater emphasis on the incidence/prevalence of concussive injuries in male athletes. We analyzed 28 published studies on sports-related concussion/mild TBI over the last 8 years. The incidence of concussion in female athletes was evaluated in less than half of these studies (13) and only three examined females exclusively. For those investigations analyzing concussions in both genders, the incidence per 1,000 athletic exposures (AE) was greater in females (.348 per 1,000 AE) as compared to males (.289 per 1,000 AE). For those studies solely investigating concussions in soccer, the female-to-male concussion ratio was nearly identical (.382 and .364 per 1,000 AE, respectively). However, when considering other sports (baseball/softball, basketball, and field hockey), the incidence of concussive injury was nearly double in females as compared to males (.293 vs. .165 per 1,000 AE). Considering these data, future investigators should not only include female athletes in their research, but should also focus on the factors associated with sports-related concussion in female athletes. We offer two potential explanations for the increased incidence/risk of concussion in female athletes: the skeletomuscular and biomechanical differences between men and women result in greater risk for women to sustain brain injury, and a socio-psychological explanation describing the differences in how males and females approach athletics, and in particular contact athletics.
Cumulative effects of concussion in amateur athletes
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The purpose of this study was to examine the possibility that athletes with multiple concussions might show cumulative effects. Amateur athletes with a history of three or more concussions ($n = 19$) were carefully matched (gender, age, education, and sport) with athletes with no prior concussions ($n = 19$). All completed a computerized neuropsychological test battery at preseason (ImPACT), and then within 5 days of sustaining a concussion (mean = 1.7 days). A mixed-model 2 x 2 ANOVA was used to determine if there were between and within group effects on the dependent variables. For total self-reported symptoms, there was a significant main effect for time ($P < .00001$, $\eta^2 = .45$). Independent group $t$-tests revealed a significant difference between groups at preseason, with the athletes who had multiple concussions reporting more symptoms ($P < .05$, $d = 0.71$, large effect). For the memory composite score, there was a significant main effect for time ($P = .001$, $\eta^2 = .27$), and a group effect, with the multiply concussed athletes showing greater decrements in memory functioning than the mildly concussed subjects ($P = .012$, $\eta^2 = .16$). Athletes with multiple concussions obtained significantly lower memory scores during the postinjury assessment ($P = .015$, $d = 0.83$, large effect). Athletes with multiple concussions were 7.7 times more likely to demonstrate a major drop in memory performance than the athletes with no previous concussions. This study provides preliminary, provocative evidence to suggest that athletes with multiple concussions might have cumulative effects.

The relationship between verbal learning patterns, injury severity, and employability following traumatic brain injury
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We examined the differences in verbal learning patterns in employed and unemployed individuals with traumatic brain injury (TBI). Existing records of individuals with mild or moderate-to-severe TBI ($n = 25$) from a regional Community Re-Entry Program were reviewed. The California Verbal Learning Test (CVLT) was used to document verbal learning patterns and employment status and change in employment status following TBI were also documented. The results did not support a relationship between verbal learning patterns and change in employment status following the injury. The lack of group differences on CVLT subscale performance illustrates potential problems involving ecological validity of neuropsychological tests with respect to employment following TBI. In our study, individuals with moderate-to-severe TBIs were more likely to return to work than those with mild TBIs. While this finding was contrary to expectations, these results are not anomalous in a clinical setting, in that the severity of impairment may not always equate to the original injury severity. Individuals with moderate-to-severe TBI and greater subsequent impairment following TBI may be more accepting of their deficits, open to clinical interventions in the form of job coaching, and more willing to entering the work force at a reduced level. In contrast, individuals with mild TBI and more subtle subsequent impairment following TBI may be less accepting or aware of their deficits, which may ultimately thwart rehabilitative efforts. Implications for these findings may be that the individual’s reaction to their injury, and level of insight, rather than injury severity variables or neuropsychological testing, mediate employment following TBI.
Background  Depression symptoms may be associated with the development of Alzheimer disease (AD). Objectives  To evaluate the association between depression symptoms and risk of AD, and to explore the temporal aspects of this association. Setting  Academic institutions with specialized memory clinics. Design  Cross-sectional, family-based, case-control study with standardized self- and proxy questionnaires to collect information on depression symptoms and other risk factors. Participants  A total of 1953 subjects with AD and 2093 of their unaffected relatives enrolled in the Multi-institutional Research in Alzheimer's Genetic Epidemiology Study. Main Outcome Measures  Odds ratios (ORs) of AD were estimated with and without depression symptoms, adjusted for age, sex, education, history of head trauma, and apolipoprotein E status. Results  There was a significant association between depression symptoms and AD (adjusted OR, 2.13; 95% confidence interval [CI], 1.71-2.67). In families where depression symptoms first occurred within 1 year before the onset of AD, the association was higher (OR, 4.57; 95% CI, 2.87-7.31), while in the families where the depression symptoms first occurred more than 1 year before the onset of AD, the association was lower (OR, 1.38; 95% CI, 1.03-1.85). In families where depression symptoms first occurred more than 25 years before the onset of AD, there was still a modest association (OR, 1.71; 95% CI, 1.03-2.82). Conclusions  Depression symptoms before the onset of AD are associated with the development of AD, even in families where first depression symptoms occurred more than 25 years before the onset of AD. These data suggest that depression symptoms are a risk factor for later development of AD.

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A saturated-fat diet aggravates the outcome of traumatic brain injury on hippocampal plasticity and cognitive function by reducing brain-derived neurotrophic factor

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Abstract
We have conducted studies to determine the potential of dietary factors to affect the capacity of the brain to compensate for insult. Rats were fed with a high-fat sucrose (HFS) diet, a popularly consumed diet in industrialized western societies, for 4 weeks before a mild fluid percussion injury (FPI) or sham surgery was performed. FPI impaired spatial learning capacity in the Morris water maze, and these effects were aggravated by previous exposure of the rats to the action of the HFS diet. Learning performance decreased according to levels of brain-derived neurotrophic factor (BDNF) in individual rats, such that rats with the worst learning efficacy showed the lowest levels of BDNF in the hippocampus. BDNF immunohistochemistry localized the decreases in BDNF to the CA3 and dentate gyrus of the hippocampal formation. BDNF has a
strong effect on synaptic plasticity via the action of synapsin I and cAMP-response element-binding protein (CREB), therefore, we assessed changes in synapsin I and CREB in conjunction with BDNF. Levels of synapsin I and CREB decreased in relation to decreases in BDNF levels. The combination of FPI and the HFS diet had more dramatic effects on the active state (phosphorylated) of synapsin I and CREB. There were no signs of neurodegeneration in the hippocampus of any rat group assessed with Fluoro-Jade B staining. The results suggest that FPI and diet impose a risk factor to the molecular machinery in charge of maintaining neuronal function under homeostatic and challenging situations.

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The amygdala is part of the behavioural reinforcement system modulating long-term potentiation in rat hippocampus

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Abstract
Long-term potentiation (LTP) in the dentate gyrus can be modulated and prolonged by emotional/motivational influences when concurrently activated. A similar effect on LTP can be obtained by stimulating the amygdala, suggesting that this limbic structure might be part of the neural system involved in behavioural reinforcement. To confirm this we have performed a series of experiments in which the basolateral amygdala was either temporary inactivated by injection of lidocaine or permanently lesioned electrolytically. Both manipulations completely blocked the reinforcing effect of a motivational stimulus (drinking after 24-h deprivation) on LTP at the perforant pathway-dentate gyrus synapses, whilst leaving intact the non-reinforced potentiation. These results demonstrate that the basolateral amygdala is a key structure within the system involved in the modulatory interaction between the affective status of the animal and the mechanisms of functional plasticity.

Functional status, neuropsychological functioning, and mood in chronic fatigue syndrome (CFS): relationship to psychiatric disorder.
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Individuals with chronic fatigue syndrome (CFS) face chronic physical debilitation, reduced neuropsychological functioning, and changes in emotional well-being that significantly detract from quality of life. The role of psychiatric disturbance in reducing quality of life in CFS remains unclear. In the current investigation, the role of psychiatric status in reducing health-related quality of life in CFS was examined. Four subject groups were compared on measures of
functional well-being, mood, and neuropsychological status: individuals with CFS and no history of psychiatric illness, individuals who had current symptoms of psychiatric illness that began after their CFS diagnosis, individuals who had current symptoms of psychiatric illness that began before their CFS diagnosis, and a healthy sedentary control group. Overall, it was found that individuals with CFS suffer from profound physical impairment. Concurrent psychiatric illness, however, did not adversely affect physical functional capacity. Physical functional capacity was not worse in individuals with a concurrent psychiatric illness. As expected, concurrent psychiatric illness was found to reduce emotional well-being. Moreover, individuals with a psychiatric illness that predated the onset of CFS suffered the greatest emotional distress. Thus, an individual's psychiatric history should be considered when attempting to understand the factors maintaining disability in CFS.

Ideal versus reality: physicians perspectives on patients with chronic fatigue syndrome (CFS) and fibromyalgia.
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Encountering patients with chronic fatigue syndrome (CFS) or fibromyalgia can cause dilemmas for physicians due to the uncertainty inherent in these illnesses. The aim of this study was to investigate: (1) How physicians in a Swedish sample describe and categorise patients with CFS and fibromyalgia; (2) What the character of CFS and fibromyalgia, with regard to diagnosing, treatment and medical knowledge/aetiology, mean to the physicians in encounters with patients; and (3) Which strategies physicians describe that they use in the encounter with these patients. Semi-structured interviews were carried out with 26 physicians, specialists in various fields who all had some experience of either CFS or fibromyalgia. The results suggest that there is a discrepancy between the ideal role of the physician and reality in the everyday work in interaction with these patients. This may lead to the professional role being questioned. Different strategies are developed to handle the encounters with these patients. The results also illuminate the physician's interpretations of patients in moralising terms. Conditions given the status of illness were regarded, for example, as less serious by the physicians than those with disease status. Scepticism was expressed regarding especially CFS, but also fibromyalgia. Moreover, it is shown how the patients are characterised by the physicians as ambitious, active, illness focused, demanding and medicalising. The patient groups in question do not always gain full access to the sick-role, in part as a consequence of the conditions not being defined as diseases.

Cortical reorganisation and chronic pain: implications for rehabilitation.
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Recent neuroscientific evidence has revealed that the adult brain is capable of substantial plastic change in such areas as the primary somatosensory cortex that were formerly thought to be modifiable only during early experience. These findings have implications for our understanding of chronic pain. Functional reorganisation in both the somatosensory and the motor system was observed in neuropathic and musculoskeletal pain. **In patients with chronic low back pain and fibromyalgia the amount of reorganisational change increases with chronicity; in phantom limb pain and other neuropathic pain syndromes cortical reorganisation is correlated with the amount of pain. These central alterations may be viewed as pain memories that influence the processing of both painful and nonpainful input to the somatosensory system as well as its effects on the motor system. Cortical plasticity related to chronic pain can be modified by behavioural interventions that provide feedback to the brain areas that were altered by somatosensory pain memories or by pharmacological agents that prevent or reverse maladaptive memory formation.**

**Fibromyalgia--from syndrome to disease. overview of pathogenetic mechanisms.**
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According to the classification criteria proposed by the American College of Rheumatology, fibromyalgia is a long-standing multifocal pain condition combined with generalised allodynia/hyperalgesia. **It is the generalised allodynia/hyperalgesia that distinguishes fibromyalgia from other conditions with chronic musculoskeletal pain. Central sensitisation of nociceptive neurons in the dorsal horn due to activation of N-methyl-D-aspartic acid receptors and disinhibition of pain due to deficient function of the descending inhibitory system are probable pathogenic factors for allodynia/hyperalgesia. Furthermore, chronic pain is a chronic emotional and physical stressor. Chronic stress and chronic sleep disturbance are not specific for fibromyalgia but could be the causes of symptoms like fatigue, cognitive difficulties and other stress-related symptoms. They may also cause neuroendocrinological and immunological aberrations.**

**Absence Epilepsy with Onset before Age Three Years: A Heterogeneous and Often Severe Condition.**
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Purpose: The classification of epilepsies and epileptic syndromes recognizes three syndromes with typical absences [TA, i.e., childhood and juvenile absence epilepsies (CAE and JAE), and epilepsy with myoclonic absences (EMA), none of which is characterized by onset in early childhood]. Although several other forms of absence epilepsies have been described recently, none concerns infants and very young children, and little is known about the nosology and prognosis of early-onset absences. Methods: We retrospectively selected all cases with onset
of absences as the only or major seizure type before age 3 years and ≥2 years of follow-up among cases newly referred between 1986 and 2002. Neuropsychological assessments (generally IQ measure), behavior patterns, and schooling situations were reviewed for each child. Results: We found 10 patients (7 F, 3 M). No child had sensory or motor deficits: neuroimaging was performed in nine and was normal in eight, with aspecific findings in one. Only two could be characterized as CAE and EMA, respectively, both with seizure control and a good cognitive outcome. Among the remaining eight cases, four had a fairly homogeneous presentation with predominantly brief absences and clearly asymmetric interictal EEGs. All eight had neuropsychological and/or behavioral difficulties. Three had full seizure control, and five, persisting absences, with a follow-up ranging between 2 years 8 months to 9 years 4 months; only one child was older than 12 years. Conclusions: Great heterogeneity exists among absence epilepsies of early onset, which are rare conditions. Only a few patients can be categorized into well-known syndromes. The overall prognosis is poor. Early onset of absences is uncommon, and multicenter studies should help clarify the nosology and prognosis.


Transcranial magnetic stimulation: studying motor neurophysiology of psychiatric disorders.
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RATIONALE. Transcranial magnetic stimulation (TMS) is a noninvasive tool that directly stimulates cortical neurons by inducing magnetic and secondary electric fields. Traditionally TMS has been used to study the motor neurophysiology of healthy subjects and those with neurological disorders. OBJECTIVE. Given the known motor dysfunctions in many psychiatric disorders supplemental usage of TMS to study the underlying pathophysiology of certain psychiatric disorders and to assess treatment outcomes is underway. Such studies include examination of motor neuronal membrane, corticospinal and intracortical excitability. Our objective is to overview the past findings. METHODS. We review the past literature that used TMS as an assessment tool in psychiatric disorders such as schizophrenia, mood disorders, Tourette's syndrome, obsessive-compulsive disorder, attention-deficit hyperactivity disorder, and substance abuse. RESULTS. While the findings are still preliminary due to small sample-size, inconsistent patient population (diagnosis, medication), differences in methodology between research groups, studies restricted to the motor region and possible lack of sensitivity and specificity, the studies are yielding interesting results which could potentially lead to trait- and state-markers of psychiatric disorders. CONCLUSIONS. Future studies using TMS alone or in combination with other neuroimaging techniques promise to further expand the application of TMS from studies of motor excitability to higher cognitive functions.


Integrative neuroscience.
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A fundamental impediment to an "Integrative Neuroscience" is the sense that scientists building models at one particular scale often see that scale as the epicentre of all brain function. This fragmentation has begun to change in a very distinctive way. Multidisciplinary efforts have provided the impetus to break down the boundaries and encourage a freer exchange of information across disciplines and scales. Despite huge deficits of knowledge, sufficient facts about the brain already exist, for an Integrative Neuroscience to begin to lift us clear of the jungle of detail, and shed light upon the workings of the brain as a system. Integrations of brain theory can be tested using judicious paradigm designs and measurement of temporospatial activity reflected in brain imaging technologies. However, to test realistically these new hypotheses requires consistent findings of the normative variability in very large numbers of control subjects, coupled with high sensitivity and specificity of findings in psychiatric disorders. Most importantly, these findings need to be analyzed and modeled with respect to the fundamental mechanisms underlying these measures. Without this convergence of theory, databases, and methodology (including across scale physiologically realistic numerical models), the clinical utility of brain imaging technologies in psychiatry will be significantly impeded. The examples provided in this paper of integration of theory, temporospatial integration of neuroimaging technologies, and a numerical simulation of brain function, bear testimony to the ongoing conversion of an Integrative Neuroscience from an exemplar status into reality.


Interface of information technology and neuropsychology: ethical issues and recommendations.
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Rapid advancements in information technology and telecommunications (ITT) offer exciting opportunities for neuropsychology. However, guidelines and recommendations for identifying and negotiating ethical challenges have not kept pace with the expansion of ITT. Because many neuropsychologists evaluate and/or treat individuals with cognitive, emotional, and/or physical limitations, neuropsychologists have a responsibility to be aware of the ethical issues associated with ITT use in order to avoid harming those who may be less able to understand or independently manipulate such technology themselves. The purpose of this paper is to raise awareness of potential implications of the interface between ethics and information technology for neuropsychologists. The first steps in this process include defining terms, identifying relevant issues and challenges, and identifying initial mechanisms to address ethical challenges. In addition, strategies for avoiding ethical misconduct related to information technology are discussed and specific recommendations are offered.

Neuroreport. 2003 Jul 1;14(9):1197-1202.

Functional neuroimaging predicts individual memory outcome after amygdalohippocampectomy.

We examined memory-related activity within to-be-resected medial temporal lobe (MTL) structures in 12 epilepsy patients with PET before amygdalohippocampectomy and studied the
reallocation of memory functions to the contralateral MTL before and after surgery. Learning tasks were designed to activate predominantly the right or left MTL. Those patients who significantly activated to-be-resected ipsilateral MTL structures during the ipsilateral learning task (i.e. the left MTL during verbal learning or the right MTL during nonverbal learning) experienced a postoperative memory decline. Preoperative activation in the contralateral MTL during the ipsilateral learning task positively correlated with the postoperative outcome for ipsilateral memory. There was no significant postoperative reallocation of ipsilateral memory functions to the contralateral MTL.

Affective disorders in neurological diseases: a case register-based study.
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OBJECTIVE: To investigate the temporal relationships between a range of neurological diseases and affective disorders. METHOD: Data derived from linkage of the Danish Psychiatric Central Register and the Danish National Hospital Register. Seven cohorts with neurological index diagnoses and two control group diagnoses were followed for up to 21 years. The incidences of affective disorders in the different groups were compared with the control groups, using competing risks to consider the risk of affective disorder and the risk of death in the same analysis. RESULTS: We found an increased incidence of affective disorders in dementia, Parkinson's disease, epilepsy, stroke and intracerebral haemorrhage compared with control groups. The association was found to be the strongest for dementia and Parkinson's disease. In hospitalized patients, with incident multiple sclerosis, the incidence of affective disorder was lower than the incidence in the control groups. CONCLUSION: In neurological diseases there seems to be an increased incidence of affective disorders. The elevated incidence was found to be particularly high for dementia and Parkinson's disease (neurodegenerative diseases).

Alterations in brain activation in posttraumatic stress disorder patients with severe hyperarousal symptoms and impulsive aggressiveness.
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OBJECTIVE: We wanted to assess possible alterations in brain activation in PTSD patients with severe hyperarousal symptoms and impulsive aggressiveness. METHOD: 25 Croatian War (1991-1995) veterans with combat-related PTSD with severe hyperarousal symptoms and impulsive aggressiveness were assessed for possible alterations in cerebral blood flow in single photon emission computed tomography brain scans. RESULTS: Increased regional cerebral blood flow in projection area of nucleus accumbens was found in 13 of 25 subjects, and for all in the dominant brain hemisphere. DISCUSSION: We believe that at least
some of PTSD symptoms, and especially the impulsive aggression, can be associated with increased regional cerebral blood flow in the projection area of nucleus accumbens.

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Right Frontal Brain Activity, Cortisol, and Withdrawal Behavior in 6-Month-Old Infants
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Richard J. Davidson

Although several studies have examined anterior asymmetric brain electrical activity and cortisol in infants, children, and adults, the direct association between asymmetry and cortisol has not systematically been reported. In nonhuman primates, greater relative right anterior activation has been associated with higher cortisol levels. The current study examines the relation between frontal electroencephalographic (EEG) asymmetry and cortisol (basal and reactive) and withdrawal-related behaviors (fear and sadness) in 6-month-old infants. As predicted, the authors found that higher basal and reactive cortisol levels were associated with extreme right EEG asymmetry. EEG during the withdrawal–negative affect task was associated with fear and sadness behaviors. Results are interpreted in the context of the previous primate work, and some putative mechanisms are discussed.


Fluvoxamine Reduces Responsiveness of HPA Axis in Adult Female BPD Patients with a History of Sustained Childhood Abuse
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The aim of the study is to test whether fluvoxamine affects the function of the hypothalamic pituitary adrenal (HPA) axis in female borderline (borderline personality disorder, BPD) patients with and without a history of sustained childhood abuse. Special attention is given to the presence of comorbid major depressive disorder (MDD) and post-traumatic stress disorder (PTSD). The HPA axis of 30 female BPD patients with (n=17) and without (n=13) a history of sustained childhood abuse was challenged with a combined dexamethasone and corticotropin releasing hormone test (DEX/CRH test) before and after 6 (n=14) and 12 (n=16) weeks of fluvoxamine treatment (150 mg/day). Both 6- and 12-week fluvoxamine treatments were associated with a significant and robust reduction of the adrenocorticotropic hormone (ACTH) and cortisol response to the DEX/CRH test. The magnitude of the reduction was dependent on the presence of sustained childhood abuse, but not on the presence of comorbid MDD or PTSD: patients with a history of sustained childhood abuse showed the strongest reduction in ACTH and cortisol. In conclusion, Fluvoxamine treatment reduces the hyperresponsiveness of the HPA axis in BPD patients with a history of sustained childhood abuse. This effect is likely to be obtained in the first 6 weeks of treatment.
Anxious-Retarded Depression: Relation with Plasma Vasopressin and Cortisol
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Dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis is related to melancholic or endogenous depression; however, the strength of this relationship depends on the definition of the specific depression subcategory. A two-dimensionally defined subcategory, anxious-retarded depression, is related to melancholic depression. Since arginine vasopressin (AVP) activates the HPA axis, and both major depression and the melancholic subcategory are associated with elevated plasma AVP levels, we investigated whether the plasma AVP level is also elevated in anxious-retarded depression, melancholic depression and anxious-retarded melancholic depression, and whether plasma AVP and cortisol levels are correlated in these subcategories. A total of 66 patients with major depression not using oral contraception were investigated. Patients with anxious-retarded depression had a highly significant AVP-cortisol correlation, while no such correlation was found in patients with nonanxious-retarded depression. Log-transformed mean plasma AVP values were higher in patients with anxious-retarded depression than in patients with nonanxious-retarded depression. Patients with anxious-retarded melancholic depression also had a significantly elevated level of plasma AVP and a highly significant correlation between plasma AVP and cortisol levels. The correlation was low in patients with melancholic depression. Anxious-retarded depression may be a useful refinement of the melancholic subcategory with regard to dysregulation of the HPA axis and plasma AVP release.

Acute SSRI Administration Affects the Processing of Social Cues in Healthy Volunteers
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Enhancement of serotonin neurotransmission plays an important role in the antidepressant response to agents presently available to treat depression. This response forms the major evidence for the role of serotonin in affective and social behaviour in humans. The present study investigated the effects of acute administration of the selective serotonin reuptake inhibitor (SSR1), citalopram (10 mg, i.v.) upon a measure of emotional processing in healthy female volunteers. Subjects completed a facial expression recognition task following infusion of citalopram or saline (between-subjects design, double-blind). Facial expressions associated with five basic emotions (happiness, sadness, fearfulness, anger and disgust) were displayed. Each face had been 'morphed' between neutral (0%) and each emotional standard (100%) in 10% steps, leading to a range of emotional intensities. Mood and subjective experience were also monitored throughout the testing session. Volunteers receiving citalopram detected a higher number of facial expressions of fear and happiness, with reduced response times, relative to those given the placebo. By contrast, changes in the recognition of other basic emotions.
were not observed following citalopram. Notable differences in mood were also not apparent in these volunteers. These results suggest that acute administration of antidepressant drugs may affect neural processes involved in the processing of social information. This effect may represent an early acute effect of SSRIs on social and emotional processing that is relevant to their therapeutic actions.


The Role of Lipid-Lowering Drugs in Cognitive Function: A Meta-Analysis of Observational Studies
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Study Objective: To quantify the risk of cognitive impairment with use of lipid-lowering drugs. Design and Data Sources: Literature search through MEDLINE and EMBASE databases; data from seven observational studies were analyzed.

Measurements and Main Results: We quantified the risk of cognitive impairment first with the use of any lipid-lowering drug, and then specifically with the statins, using the random effects model. We tested for heterogeneity using the Q statistic as well as quantitatively using the Ri statistic. All seven studies provided data for statin users, and five provided data only on use of lipid-lowering drugs. Compared with patients not receiving lipid-lowering drugs, the relative risk of cognitive impairment with any lipid-lowering drug was 0.62 but was not statistically significant (95% confidence interval [CI] 0.28-1.38), and the relative risk with statins was 0.43 and was statistically significant (95% CI 0.31-0.62). Conclusion: Lipid-lowering drugs -- in particular, the statins -- seem to lower the odds of developing cognitive impairment. Randomized, controlled trials are needed to address the efficacy of these agents specifically in different types of dementia.


Neurofeedback treatment for attention-deficit/hyperactivity disorder in children: a comparison with methylphenidate.
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Clinical trials have suggested that neurofeedback may be efficient in treating attention-deficit/hyperactivity disorder (ADHD). We compared the effects of a 3-month electroencephalographic feedback program providing reinforcement contingent on the production of cortical sensorimotor rhythm (12-15 Hz) and betal activity (15-18 Hz) with stimulant medication. Participants were N = 34 children aged 8-12 years, 22 of which were assigned to the neurofeedback group and 12 to the methylphenidate group according to their parents' preference. Both neurofeedback and methylphenidate were associated with improvements on all subscales of the Test of Variables of Attention, and on the speed and accuracy measures of the d2 Attention Endurance Test. Furthermore, behaviors related to
the disorder were rated as significantly reduced in both groups by both teachers and parents on the IOWA-Conners Behavior Rating Scale. These findings suggest that neurofeedback was efficient in improving some of the behavioral concomitants of ADHD in children whose parents favored a nonpharmacological treatment.

Clinical correlates of aggressive behavior after traumatic brain injury.
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The authors assessed aggressive behavior in 89 patients with traumatic brain injury (TBI) and 26 patients with multiple trauma but without TBI using a quantitative scale (the Overt Aggression Scale) and examined its clinical correlates. Aggressive behavior was found in 33.7% of TBI patients and 11.5% of patients without TBI during the first 6 months after injury. Aggressive behavior was significantly associated with the presence of major depression, frontal lobe lesions, poor premorbid social functioning, and a history of alcohol and substance abuse. Interventions aimed at treatment of depression and substance abuse and enhancing social support may help reduce the severity of this disruptive behavior.

Functional neuroimaging studies of motor recovery after stroke in adults: a review.
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BACKGROUND: The precise mechanisms of and biological basis for motor recovery after stroke in adults are still largely unknown. Reorganization of the motor system after stroke as assessed by functional neuroimaging is an intriguing but challenging new field of research. Provocative but equivocal findings have been reported to date. SUMMARY OF REVIEW: We present an overview of functional neuroimaging studies (positron emission tomography or functional MRI) of motor tasks in patients recovered or still recovering from motor deficit after stroke. After a brief account of the connectivity of motor systems and the imaging findings in normal subjects, the literature concerning stroke patients is reviewed and discussed, and a general model is proposed. CONCLUSIONS: Both cross-sectional and longitudinal studies have demonstrated that the damaged adult brain is able to reorganize to compensate for motor deficits. Rather than a complete substitution of function, the main mechanism underlying recovery of motor abilities involves enhanced activity in preexisting networks, including the disconnected motor cortex in subcortical stroke and the infarct rim after cortical stroke. Involvement of nonmotor and contralesional motor areas has been consistently reported, with the emerging notion that the greater the involvement of the ipsilesional motor network, the better is the recovery. This hypothesis is supported by the enhanced activity of the ipsilesional primary motor cortex induced by motor training and acute pharmacological interventions, in parallel with improved motor function. Further
longitudinal studies assessing the relationships between such changes and actual recovery, as well as manipulating such changes by rehabilitation or pharmacological maneuvers, should provide further information on these fundamental questions. This review closes with some perspectives for future research.

Rightward cerebral asymmetry in subtypes of schizophrenia according to Leonhard's classification and to DSM-IV: a structural MRI study.
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Although well documented, brain structural abnormalities in schizophrenia are non-specific, and morphometric parameters show significant overlap between patients and healthy controls. Such inconsistencies in neuroimaging findings could represent different levels of severity along a single pathogenic process or distinct clinical and etiopathological psychoses within a schizophrenic spectrum. The aim of the present study was the investigation of distinct brain abnormalities in different subtypes of schizophrenia. Forty patients were classified according to DSM-IV and Leonhard's classifications. Psychopathology was assessed by the Positive and Negative Syndrome Scale (PANSS) and the Negative Symptom Rating Scale (NSRS). Patients were compared to 20 healthy volunteers on volumetric measures of cerebral structures (hemisphere, hippocampus and planum temporale) and ventricular-brain ratio (VBR) obtained by magnetic resonance imaging. Patients showed rightward asymmetry of cerebral hemispheres and increased VBR. Rightward asymmetry correlated with severity of negative symptoms and prevailed in the systematic forms of Leonhard, suggesting a distinct pattern of left hemisphere abnormality in this subgroup of psychoses. Increased VBR values showed a single normal distribution in the subgroups, indicating that ventricular enlargement is not restricted to a subgroup but is present to a certain degree in all cases.

Multisensory integration after traumatic brain injury: a reaction time study between pairings of vision, touch and audition.
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Traumatic brain injury (TBI) frequently results in deficits in attention and speed of information processing. In order to disentangle the influence of sensory-specific factors and the role of cross-modal integration from the supra-modal aspects of cognitive slowing, the present reaction time (RT) study was designed. Simple and choice RT to pairings of visual, auditory and tactile stimuli were measured in 35 TBI patients and 35 matched controls. Results proved a strong influence of sensory-specific and cross-modal factors in the RTs. The tactile modality was more difficult to integrate with the visual and the auditory modality, rather than the visual and the auditory modalities between them. TBI patients showed prolonged simple and choice RTs throughout all tasks, but their difficulty with integrating the tactile modality was disproportionally higher in comparison to controls.
Tulsky, David S. 1,2,4; Price, Larry R. 3

During the standardization of the Wechsler Adult Intelligence Scale (3rd ed.; WAIS-III) and the Wechsler Memory Scale (3rd ed.; WMS-III) the participants in the normative study completed both scales. This "co-norming" methodology set the stage for full integration of the 2 tests and the development of an expanded structure of cognitive functioning. Until now, however, the WAIS-III and WMS-III had not been examined together in a factor analytic study. This article presents a series of confirmatory factor analyses to determine the joint WAIS-III and WMS-III factor structure. Using a structural equation modeling approach, a 6-factor model that included verbal, perceptual, processing speed, working memory, auditory memory, and visual memory constructs provided the best model fit to the data. Allowing select subtests to load simultaneously on 2 factors improved model fit and indicated that some subtests are multifaceted. The results were then replicated in a large cross-validation sample (N = 858).

Schoenberg, Mike R. 1,3; Dorr, Darwin 1; Morgan, C Don 2
The Ability of the Millon Clinical Multiaxial Inventory-Third Edition to Detect Malingering
This study investigated the ability of the Millon Clinical Multiaxial Inventory-Third Edition (MCMI-III) to discriminate students malingering psychopathology (n = 106) from bona fide psychiatric inpatients (n = 202). Students were randomly assigned to a fake-bad or an honest-responding condition. Analyses investigated the ability of the modifier indices to discriminate fake-bad group participants from the psychiatric inpatients. Scale X raw cutoff score > 178 yielded a positive predictive power (PPP) of 0.0, a negative predictive power (NPP) of 63.1, and a hit rate of 63.1%. Optimal cutoff scores were developed. Scale X Base Rate (BR) > 84 provided a PPP of 55.6, an NPP of 72.1, and a hit rate of 65.2%. Scale Y BR < 26 yielded a PPP of 52.5 and a hit rate of 64.8%. Receiver operating characteristic analyses found that Scale X best classified malingerers. Overall, the MCMI-III modifier indices were of minimal clinical utility in distinguishing college student malingerers from bona fide psychiatric inpatients.

Clark, Michael E. 1,2,3,7; Gironda, Ronald J. 4,5; Young, Robert W. 3,5
Detection of Back Random Responding: Effectiveness of MMPI-2 and Personality Assessment Inventory Validity Indices.
Two experiments examined the detection and effects of back random responding (BRR) on the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) and the Personality Assessment Inventory (PAI). Experiment 1 revealed that MMPI-2 Clinical and Content scales were relatively
resistant to the effects of BRR. \( F_b - F \geq 20 \) T was the most effective index for identifying invalid protocols. Experiment 2 revealed greater susceptibility of the PAI interpretive scales to the effects of BRR and less successful detection of BRR. The most effective PAI validity index was the combined indicator, ICN \( \geq 73 \) T or INF \( \geq 75 \) T. Clinical and empirical implications of these findings are discussed, and tentative modifications to the MMPI-2 interpretative guidelines are provided.

Gomez, Rapson 1; Leonard Burns, G 2,4; Walsh, James A. 3; Alves de Moura, Marcela 2

**A Multitrait-Multisource Confirmatory Factor Analytic Approach to the Construct Validity of ADHD Rating Scales.** [Article]


Confirmatory factor analysis was used to model a multitrait-multisource design to evaluate the construct validity of attention-deficit/hyperactivity disorder (ADHD) rating scales. The 2 trait factors were the ADHD inattention and hyperactivity/impulsivity dimensions. The 2 source factors were parents and teachers. In Study 1, parents and teachers rated 1,475 Australian elementary school children on the ADHD symptoms. In Study 2, parents and teachers rated 285 Brazilian elementary school children on the ADHD symptoms. Similar results occurred in both studies with most of the ADHD symptoms containing more source than trait variance, thus providing weak evidence for the convergent and discriminant validity of the symptoms as measured by rating scales. The study outlines the implications of such strong source effects for understanding ADHD.

Wilde, Nancy J. 1,7; Strauss, Esther 1; Chelune, Gordon J. 2; Hermann, Bruce P. 3; Hunter, Michael 1; Loring, David W. 4; Martin, Roy C. 5; Sherman, Elisabeth M. S. 6

**Confirmatory Factor Analysis of the WMS-III in Patients With Temporal Lobe Epilepsy.** [Article]


Five competing models specifying the factor structure underlying the Wechsler Memory Scale-Third Edition (D. Wechsler, 1997b) primary subtest scores were evaluated in a sample of patients with intractable temporal lobe epilepsy \((N = 254)\). Models specifying separate immediate and delayed constructs resulted in inadmissible parameter estimates and model specification error. There were negligible goodness-of-fit differences between a 3-factor model of working memory, auditory memory, and visual memory and a nested-more parsimonious-2-factor model of working memory and general memory. **The results suggest that specifying a separate visual memory factor provides little advantage for this sample—an unexpected finding in a population with lateralized dysfunction, for which one might have predicted separate auditory and visual memory dimensions.**
Coaching and the ability to simulate mild traumatic brain injury symptoms.
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This study assessed the ability of normal controls to simulate mild traumatic brain injury with or without the aid of general simulation strategies. An additional purpose was to evaluate the relative ability of four tests of performance motivation or malingering to discriminate among the five groups in this study. Twenty-one patients with documented mild traumatic brain injury (TBI) and 112 undergraduate students were administered the measures of symptom validity in randomized order with instructions either to perform to the best of their ability or to fake believable deficits. Students asked to malinger were either given instructions to do so with no guidance (No Strategies group or NS), a minimal level of guidance (Only Strategies group or OS) or a moderate level of guidance (Strategies and Example or SE). Students given simulation strategies (OS and SE groups) were able to match performance of the TBI group in only those instances when TBI performance was similar to the normal comparison group. When TBI performance fell considerably below the normal comparison group, naive simulators (NS group) best approximated TBI performance. The degree of variability in the classification success of the four tests underscored the necessity of combining detection methods, as well as the need to develop new tests more resistant to attempts to feign brain injury.


Two-alternative forced-choice digit recognition procedures have been the most widely employed for detecting incomplete effort and exaggeration of cognitive impairment. Other forced-choice tests based on word or picture recognition are also commonly used. However, it cannot be assumed that patients will be equally likely to fail different symptom validity tests (SVTs), whether the test involves digit recognition or some other procedure, such as word recognition memory. In this study, 519 patients referred for disability or personal injury related assessments were administered three SVTs, one based on digit recognition (Computerized Assessment of Response Bias, CARB), one using visual stimuli (Test of Memory Malingering, TOMM) and one employing verbal recognition memory (Word Memory Test, WMT). More than twice as many people failed the WMT than TOMM. CARB failure rates were intermediate between those on the other two tests. Thus, tests of recognition memory using
digits, pictorial stimuli or verbal stimuli, all of which are objectively extremely easy tasks, resulted in widely different failure rates. This suggests that, while these tests may be highly specific, they vary substantially in their sensitivity to response bias.

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Attentionally modulated effects of cortisol and mood on memory for emotional faces in healthy young males
J. Van Honk, a, R. P. C. Kesselsb, P. Putmana, G. Jagerc, b, H. P. F. Koppeschaard and A. Postmab

Heightened cortisol levels due to stress or acute administration seem to enhance memory for emotional material, independently of emotional valence. An arousal-driven neurobiological mechanism involving the amygdala has been proposed. The relation between pre-task salivary measures of cortisol (by convention named 'basal levels') and emotionally modulated memory has not been investigated yet. Given the association between higher basal levels of cortisol and indices of low mood, valence-specific effects on emotionally modulated memory could be expected (e.g. mood-congruent or stimulus-specific forms of processing). This study was designed to investigate the relationship between basal levels of salivary cortisol, self-reported mood and spatial memory for neutral, happy and angry facial expressions in healthy young volunteers (N=31). Memory performance was indexed using a modified version of a computerized object-relocation task, using emotional facial expressions as stimuli. Results showed a significant relation between cortisol and depressive mood. More importantly, both the levels of cortisol and depressive mood were inversely related to the memory performance for the happy facial expressions, while a similar relationship between cortisol and memory performance on angry faces neared significance. An explanation in terms of the down-regulation of social behavior by elevated basal cortisol levels is postulated.

Psychiatry Research: Neuroimaging
Article in Press, Corrected Proof - Note to users

Impulsivity and prefrontal hypometabolism in borderline personality disorder
Paul H. Soloff, a, Carolyn Cidis Meltzerb, Carl Beckerb, Phil J. Greerb, Thomas M. Kellya and Doreen Constantinea

Prefrontal hypoperfusion and decreased glucose uptake in the prefrontal cortex (PFC) are found in violent criminal offenders, murderers and aggressive psychiatric patients. These abnormalities may be independent of diagnosis and associated with impulsive-aggression as a personality trait. Impulsive-aggression is a clinical characteristic of borderline personality disorder (BPD) where it is associated with assaultive and suicidal behaviors. We conducted FDG-PET studies in 13 non-depressed, impulsive female subjects with BPD and 9 healthy controls to look for abnormalities in glucose metabolism in areas of the PFC associated with regulation of impulsive behavior. Statistical Parametric Mapping-99 (was used to analyze the PET data with Hamilton depression scores as covariate. Significant reductions in FDG uptake in BPD subjects relative to healthy controls were found bilaterally in medial orbital frontal cortex,
including Brodmann's areas 9, 10 and 11. There were no significant areas of increased uptake in BPD subjects compared to control subjects. Covarying for measures of impulsivity or impulsive-aggression rendered insignificant the differences between groups. Decreased glucose uptake in medial orbital frontal cortex may be associated with diminished regulation of impulsive behavior in BPD.

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**Single-voxel proton MR spectroscopy of right versus left hippocampi in PTSD**
P. Mohanakrishnan Menon, , c, Henry A. Nasrallah, b, Judith A. Lyons, b, Mertis F. Scott and Vincent Liberto, b

Previous magnetic resonance (MR) volume imaging and proton MR spectroscopy studies have suggested a reduction in the hippocampal size and/or neuronal/axonal density in posttraumatic stress disorder (PTSD). The lack of agreement on the laterality of the hippocampal dysfunction prompted this study. A total of 20 veterans (18 men and two women) and one female non-veteran participated in this study conducted in accordance with approved human study protocols. Six of the male veterans and the female non-veteran were without PTSD. Vietnam veterans formed a large subset of the study subjects. Single-voxel proton MR spectra were obtained from the hippocampal region bilaterally on a clinical MR scanner operating at 1.5 T. Analysis of the proton MR spectra showed a decrease in hippocampal NAA/creatine ratio in PTSD subjects significantly higher on the left than the right for the entire study group, as well as for the Vietnam subset. **It was concluded that the hippocampal dysfunction in PTSD is lateralized with the left side being more impaired than the right.**

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**Neuropsychological correlates of P300 abnormalities in patients with schizophrenia and obsessive–compulsive disorder**
Myung-Sun Kim, Seung-Suk Kang, Tak Youn, b, Do-Hyung Kang, Jae-Jin Kim and Jun Soo Kwon, , a, b

The cognitive significance of P300 abnormalities in schizophrenia and obsessive–compulsive disorder (OCD) was investigated. P300 was measured by an auditory oddball paradigm, in which a series of standard tones (1000 Hz) and target tones (1500 Hz) were presented. The subject's task was to count the number of the presented target tones. Cognitive functions were evaluated by neuropsychological tests, which were chosen to be sensitive to frontal and temporal dysfunction. Twenty-two schizophrenic patients, 19 OCD patients and 21 healthy controls participated. Event-related potentials measured at 15 electrode sites, which consisted of five levels on the left–right dimension and three levels on the anterior–posterior dimension, were included in the statistical analysis. P300 amplitudes on all 15 electrode sites were significantly smaller in schizophrenic and OCD patients than in the controls. Schizophrenic patients performed poorly on almost all neuropsychological tests, while OCD patients showed impaired performance on the Rey–Osterrieth Complex Figure Test and on a controlled oral word association test. In schizophrenic patients, P300 amplitude was associated with performance on...
verbal memory and learning by the Luria–Nebraska Neuropsychological Battery, while for OCD patients, P300 amplitude was related to the Trail Making Test, Part B response time. These results indicate that schizophrenic patients have generalized cognitive impairments, which are substrated by a wide range of cortical dysfunctions. **The major cognitive deficits observed in OCD patients were impairments of controlled attention and self-guided, flexible behavior, which are mediated by the fronto-striatal system.** The neurophysiological mechanisms underlying P300 abnormalities observed in schizophrenic and OCD patients are discussed.