Schizophrenia

**SCZ, Violence, Olanzapine & Risperidone**

- Reducing violence risk in persons with schizophrenia: **Olanzapine versus risperidone.**

**Authors:** Swanson JW, Swartz MS, Elbogen EB, Van Dorn RA.
- From the Services Effectiveness Research Program, Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, N.C.

**Source:** J Clin Psychiatry. 2004 Dec;65(12):1666-73. Related Articles, Links

**Summary:** This study prospectively examined the effectiveness of treatment with olanzapine versus risperidone in reducing violent behavior among patients with schizophrenia under "usual care" conditions in the community. METHOD: Participants were 124 adults with DSM-IV-diagnosed schizophrenia-spectrum disorders receiving services in public-sector mental health systems in North Carolina. After enrollment (1997-1999), subjects were followed for 3 years in an observational study with interviews at 6-month intervals to assess treatment, clinical outcomes, and violent behavior. Rates of violence were compared over time between periods of first switch to olanzapine or risperidone and periods following at least 1 year of treatment with each of these medications. RESULTS: The study found that remaining on olanzapine for 1 year or more significantly lowered violence risk compared to first switch period, but no significant change in violence risk was found for subjects remaining on risperidone for 1 year or more. These results were obtained using multivariable time-series analysis controlling for salient demographic and clinical covariates. **Conclusion:** This study found that, in the complex "real world" settings where persons with schizophrenia reside, long-term treatment with olanzapine confers some advantage over risperidone in reducing violence risk. This advantage appears to be at least in part an indirect effect, via improvement in adherence with treatment. Specifically, adherence with prescribed medication was found to mediate the association between olanzapine treatment and reduced violent behavior.

Olanzapine & Schizophrenia simplex

- **[A Patient Who for One Year Shared his Apartment with his Dead Ladyfriend’s Corpse.]**

**Authors:** Niethammer R, Taubert E, Breitmaier J. - Abteilung fur Psychiatrie und Psychotherapie, Krankenhaus Zum Guten Hirten Ludwigshafen

**Source:** Psychiatr Prax. 2005 Jan;32(1):39-41. Related Articles, Links

**Summary:** A 58-year old unemployed painter had for one year shared his apartment with his ladyfriend's corpse and not talked to anyone about her death. When admitted to our hospital, loss of drive, initiative, interest, psychomotor activity and emotional response as well as poverty of speech were the main clinical features. Not having been able to care for his own vital needs such as food, shelter and protection against cold temperature, he was neglected and suffered from frostbites. We diagnosed a schizophrenia simplex and initiated neuroleptic treatment using olanzapine. During the course of treatment there was some improvement regarding affect and psychomotor activity, his loss of drive and initiative and indifference regarding his own situation in life did hardly improve.

Arabpsynet eJournal: N°6 - April - May - June 2005
SCZ, Cognitive functions & Quetiapine

* Effects of quetiapine on cognitive functions in schizophrenia.

**Authors:** Kivrıcik Akdede BB, Aiptekin K, Kitis A, Arkar H, Akvardar Y. - Department of Psychiatry, Dokuz Eylul University School of Medicine, Balcova, Inciralti Izmir, Turkey.


**Summary:** OBJECTIVE: All atypical antipsychotic drugs with complex pharmacology have been shown to improve some, but not all, domains of cognitive function, including quetiapine, i.e., the agent with the most rapid dissociation from dopamine receptors and a relatively weak serotonin antagonism. The present study was designed to evaluate which, if any, areas of cognition improve in patients with schizophrenia, following a brief treatment with quetiapine. METHODS: Effects of quetiapine on cognition were investigated in a group of patients with schizophrenia (n=14). Neuropsychological tests in cognitive areas previously shown as impaired in schizophrenia were administered at baseline and after 8 weeks of treatment with quetiapine. Administered at these two times were also the Positive and Negative Syndrome Scale, Hamilton Depression Rating Scale, and scales to assess motor side effects (Abnormal Involuntary Movement Scale, Simpson-Angus Scale, and Barnes Akathisia Scale). RESULTS: Wilcoxon Signed Ranks Test indicated a statistically significant improvement in scores on Digit Span Test, Trail Making Test, Stroop Test, Finger Tapping Test, and on the Positive and Negative Syndrome Scale. No significant change was noted in motor side effects. Conclusion: The patients improved in their attentional, motor, and visuo-motor skills, and in executive functions as well as with respect to psychopathology, without an increase in motor side effects.

SCZ, Haloperidol & Allopurinol

* Beneficial antipsychotic effects of allopurinol as add-on therapy for schizophrenia: a double blind, randomized & placebo controlled trial.

**Authors:** Akhondzadeh S, Safarcherati A, Amini H. - Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, Tehran, Iran


**Summary:** There is a large amount of data showing that adenosine plays a role opposite to dopamine in the brain. Adenosine agonists and antagonists produce behavioral effects similar to dopamine antagonists and dopamine agonists, respectively. Allopurinol, a well-known hypouricemic drug that inhibits xantine oxidase, has been used as an add-on drug in the treatment of poorly responsive schizophrenic patients. Indeed, the neuropsychiatric effects of allopurinol in schizophrenia have been suggested to be secondary to its inhibitory effect of purine degradation, enhancing adenosinergic activity. The purpose of the present investigation was to assess the efficacy of allopurinol as an adjuvant agent in the treatment of chronic schizophrenia in an 8-week double blind and placebo controlled trial. Eligible participations in the study were 46 patients with schizophrenia. All patients were inpatients and were in the active phase of the illness, and met DSM-IV criteria for chronic schizophrenia. Patients were allocated in a random fashion, 23 to haloperidol 15 mg/day plus allopurinol 300 mg/day and 23 to haloperidol 15 mg/day plus placebo. Although both protocols significantly decreased the score of the positive, negative and general psychopathological symptoms over the trial period, the combination of haloperidol and allopurinol showed a significant superiority over haloperidol alone in the treatment of positive symptoms, general psychopathology symptoms as well as PANSS total scores. The means of Extrapyramidal Symptoms Rating Scale for the placebo group were higher than in the allopurinol group over the trial, and the differences were significant in weeks 6 and 8. A significant difference was observed between the overall mean biperiden dosages in two groups. The results of this study suggest that allopurinol may be an effective adjuvant agent in the management of patients with chronic schizophrenia. Nevertheless, results of larger controlled trials are needed, before recommendations for a broad clinical application can be made.

Bupropion SR overdose & Paranoid delusions

* Acute psychosis following sustained release bupropion overdose.

**Authors:** Wang TS, Shah IS, Yeh CB, Chang CC. - Department of Psychiatry, Tri-Service General Hospital, No 325, Sec 2, Cheng-Kung RD, Neihu District, 114, Taipei, Taiwan


**Summary:** Bupropion is an antidepressant that is structurally related to amphetamines and enhances dopamine neurotransmission through inhibiting neuronal dopamine re-uptake. Bupropion-related psychosis has been recognized in several papers, but these reports of bupropion-related psychosis almost all involve immediate release (IR) formulation. We present a case of acute psychosis following sustained release bupropion (SR) overdose. A 23-year-old male was admitted because of major depression and a suicidal attempt by ingesting 28 tablets of 150 mg bupropion SR and 14 tablets of 7.5 mg midazolam. He developed paranoid delusions 12 h after the bupropion SR overdose. The paranoid symptoms remitted on the third day of his admission. Our case of acute psychosis following bupropion SR overdose indicates the importance of being aware of the rare complication in patients receiving bupropion SR treatment.

SCZ, Ala – 9Val & Mn – SOD gene

* Association between Ala-9Val polymorphism of Mn-SOD gene & schizophrenia.

**Authors:** Akoly O, Yanik M, Elyas H, Namli M, Canatan H, Akin H, Yuce H, Yilmaz HR, Tutkun H, Sogut S, Herken H, Ozyurt H, Savas HA, Zoroglu SS. - Department of Medical Biology and Genetics, Firat University Medical School, Elazig, Turkey.

**Source:** Prog Neuropsychopharmacol Biol Psychiatry. 2005 Jan;29(1):123-31. Related Articles, Links

**Summary:** Reactive oxygen species (ROS) have been suggested to play an important role in physiopathology of schizophrenia. The major intracellular antioxidant enzymes, copper-zinc superoxide dismutase in the cytoplasm and manganese superoxide dismutase (Mn-SOD) in the mitochondria, rapidly and specifically reduce superoxide radicals to hydrogen peroxide. Polymorphisms in the genes encoding antioxidant enzymes should therefore result in predisposition to schizophrenia. The present study was performed to assess whether there is a genetic association between a functional polymorphism of Mn-SOD gene and schizophrenia.

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polymerorphism (Ala-9Val) in the human Mn-SOD gene in schizophrenic patients (n=153) and healthy controls (n=196) using a PCR/RFLP method. Significant differences in the genotypic distribution between schizophrenics and controls were observed. Genotypic distribution with 14 (9.2%) Ala/Ala, 106 (69.3%) Ala/Val and 33 (21.6%) Val/Val subjects in schizophrenia was different from those of controls with 48 (23.5%), 83 (42.3%) and 67 (34.2%), respectively (p<0.001). When the patients with schizophrenia were divided into the subgroups as disorganized, paranoid and residual, there was a significant difference in genotypic distribution among the subgroups (chi2=11.35, df=4, p=0.023). This association between -9Ala Mn-SOD allele and schizophrenia suggests that -9Ala variant may have a contribution in the physiopathogenesis of schizophrenia. Further investigations are warranted in larger populations with other susceptible genes that might be associated with schizophrenia.

SCZ, Frontal activation & Quetiapine

Restoration of frontal activation during a treatment with quetiapine: an fMRI study of blunted affect in schizophrenia.

Authors: Stip E, Fahim C, Mancini-Marie A, Bentealeb LA, Mensour B, Mendrek A, Beauregard M. - Department of Psychiatry, Centre de Recherche Fernand-Seguin, Hopital Louis-Hippolyte Lafontaine, Universite de Montreal. 7331, rue Hochelaga Montreal (Quebec), Canada H1N 3V2. emmanuel.stip@umontreal.ca


Summary: This study investigated changes in cerebral activation related to emotion processing in schizophrenia patients with blunted or flat affect (FA+) during treatment with quetiapine. Using functional magnetic resonance imaging (fMRI), brain activation in 12 FA+ schizophrenia patients during passive viewing of sad film excerpts was studied before and after a median of 5.5-months treatment with quetiapine. Random-effects paired sample t-test analyses of brain activation before quetiapine (contrast=sad-neutral, before-after) revealed significant activation in the brainstem (pons, medulla). After quetiapine, the same contrast showed significant prefrontal activation (BA 9, 10 and 11). Activation of key prefrontal areas involved in emotion processing and significant symptoms improvement as measured by the subjective rating scale and PANSS suggests the potential effect of quetiapine in improving blunted affect related symptoms (i.e., passive withdrawal, emotional withdrawal, social avoidance) in schizophrenia.

SCZ, Celiac disease & Genes

Gene, gut and schizophrenia: the meeting point for the gene-environment interaction in developing schizophrenia.

Authors: Wei J, Hemnings GP. - Schizophrenia Association of Great Britain, Institute of Biological Psychiatry, Bryn Hyfryd, The Crescent, Bangor LL57 2AG, UK


Summary: Both schizophrenia and celiac disease involve a genetic component. Several lines of evidence have shown a genetic relationship between these two conditions. Celiac disease is characterized by damage to the microscopic finger-like projections called villi, which line the small intestine and play a significant role in digestion, due to an inflammatory condition caused by a reaction to wheat gluten or related rye and barley proteins. Celiac disease represents not only malabsorption leading to a poor nutritional condition but also an alteration of gut permeability. Individuals with a history of childhood celiac condition have a raised risk of developing schizophrenia. Psychotic symptoms often occur in adult celiac disease. It can be hypothesized that apart from malnutrition, the meeting point for the gene-environment interaction may be an alteration in gut permeability, in which the gut may lose its capacity to block exogenous psychosis-causing substances that may enter the body thus causing the development of schizophrenia and other mental conditions. To support this hypothesis, the conditional test was conducted to look at the combined effect of the CLDN5 gene involved in forming permeability barriers and the DQB1 gene that has been found to be associated with celiac disease. The results demonstrate that these two genes possibly work together in conferring a susceptibility to schizophrenia.
SCZ & Impaired in memory

- Schizophrenic patients are impaired in memory reinstatement underlying mismatch negativity system.

**Authors:** Minami Y, Kirino E. - Department of Psychiatry, Juntendo University School of Medicine, 560 Fukuyoyama, Koshigayashi, Saitama 3430032, Japan.

**Source:** Clin Neuropsychol. 2005 Jan;116(1):120-8. Related Articles, Links

**Summary:** OBJECTIVE: We modified the paradigm used in the report of Cowan et al. [J Exp Psychol Learn Mem Cogn 19 (1993) 909] to investigate how the silent intervals influence the memory trace underlying mismatch negativity (MMN) generation in schizophrenic patients. METHODS: Experiment 1 was designed to explore how long an inter-train interval would be needed for the memory to become dormant. Experiment 2 was designed to elucidate how many standard stimuli would be needed to reinstate the memory. RESULTS: In Experiment 1, schizophrenic patients showed a significant reduction in MMN amplitude after the longer inter-train intervals compared to the shorter ones, although little difference was observed in controls. Specifically, the memory trace underlying the MMN system in the schizophrenic patients easily became dormant after the extended silent intervals. In Experiment 2, we could not conclude that schizophrenic patients needed more reminders than did controls in order to reinstate the memory once the memory trace became dormant. The patients might be little impaired with respect to forming the memory trace.

Conclusions: In schizophrenic patients, the memory trace in MMN generation might easily become out of context after silent intervals. Patients could not effectively reinstate the memory that was put out of context by the extended silent interval.

SIGNIFICANCE: This article provides some suggestions in terms of patients’ difficulty encoding episodes and retrieving them within distinct contexts in preconscious processes.

SCZ & Susceptibility genes

- [In search of susceptibility genes for schizophrenia] (Article in German)

**Authors:** Schosser A, Aschauer HN. - Klinische Abteilung für Allgemeine Psychiatrie, Universitätsklinik für Psychiatrie, Wien, Österreich, alexandra.schosser@meduniwien.ac.at

**Source:** Wien Klin Wochenschr. 2004 Dec 30;116(24):827-33. Related Articles, Links

**Summary:** After the recent discovery and replication of several schizophrenia candidate regions on multiple chromosomes, susceptibility genes for schizophrenia could be identified for the first time. Each of these discoveries resulted from association studies within chromosomal regions first identified by linkage analyses. Within the last two years, the susceptibility genes Neuregulin1, Dysbindin, D-amino-acid- oxidase (DAAO) and G72 were discovered, which, in the variant forms, reduce glutamatergic activity in brain. Therefore, they are related to the so-called “Glutamate-hypothesis”, which postulates a hypofunction of the glutamatergic system. Adults with VCFS (velo-cardio-facial-syndrome), where a deletion on chromosome 22q11 can be found, show a very high incidence of schizophrenia. In addition, 2% of patients with schizophrenia exhibit this 22q11-deletion. Within the VCFS-deleted region on chromosome 22q11, the genes coding for proline dehydrogenase (PRODH) and catechol-O-methyltransferase (COMT) were also found to be significantly associated with schizophrenia. Proline is a pre-stage of glutamate, and in addition, it seems to be a neuromodulator of glutamatergic transmission in the brain. COMT is one of the two enzymes degrading catecholamines such as dopamine. Therefore, it plays a large role in the cortical dopamine metabolism. Furthermore, an association of schizophrenia with the gene RGS4 (regulator-of-G-protein-signaling-4), a modulator of the function of multiple G-protein-linked neurotransmitter receptors, was identified. Gene-expression- Analyses of postmortem cerebral cortex (prefrontal) indicate that the transcription of RGS4 is diminished within schizophrenics. In accordance with the fact that schizophrenia is a disease with a multifactorial etiology, it should be emphasized that the described biological risk factors can increase susceptibility, but that none of them can cause the disease alone.

SCZ, APD & Neuropsychological profiles

- A neuropsychological investigation into violence and mental illness


**Source:** Schizophr Res. 2005 Apr 1;74(1):1-13. Related Articles, Links

**Summary:** Previous research has reported cognitive impairment in patients with schizophrenia and antisocial personality disorder (APD), the two psychiatric illnesses most implicated in violent behaviour. Previous studies have focused on either group exclusively, and have been criticized for procedural inadequacies and sample heterogeneity. The authors investigated and compared neuropsychological profiles of individuals with APD and violent and nonviolent individuals with schizophrenia in a single investigation. The study involved four groups of subjects: (i) individuals with a history of serious violence and a diagnosis of APD, (ii) individuals with a history of violence and schizophrenia, (iii) individuals with schizophrenia without a history of violent behaviour and (iv) healthy control subjects. All study groups were compared on a neuropsychological battery designed to assess general intellectual function, executive function, attention, and processing speed. Cognitive deficits were more widespread among individuals with schizophrenia regardless of history of violence, compared with those with APD. Significant impairment in patients with APD was limited to processing speed. Violent individuals with schizophrenia demonstrated poorer performance than their nonviolent schizophrenia peers on a measure of executive function. Different cognitive impairments are manifested by individuals with APD and schizophrenia with violent behaviours, suggesting differences in underlying pathology. Furthermore, cognitive impairment appears to be more a feature of schizophrenia than of violent behaviour, although there is evidence that a combination of schizophrenia...
and violent behaviour is associated with greater cognitive deficits.

**Aripiprazole, SCZ & Maintenance therapy**

- **Aripiprazole: a new atypical antipsychotic with a different pharmacological mechanism.**

  **Authors:** Naber D, Lambert M. - Department of Psychiatry and Psychotherapy, Universitätsklinikum Hamburg-Eppendorf, Martinistrasse 52, Hamburg 20246, Germany. naber@uke.uni-hamburg.de

  **Source:** Prog Neuropsychopharmacol Biol Psychiatry. 2004 Dec;28(8):1213-9. Related Articles, Links

  **Summary:** Aripiprazole is a new atypical antipsychotic with a mode of action that is distinct from currently available antipsychotic drugs. In phase III comparative clinical studies, aripiprazole 15-30 mg/day was at least as effective as haloperidol and risperidone in short term treatment of acute exacerbation of schizophrenia but superior to haloperidol in long term maintenance therapy. Consistent with an atypical profile, aripiprazole is effective against positive, negative and cognitive symptoms of schizophrenia and has a favourable side effect profile with the incidence of extrapyramidal symptoms (EPS) comparable to placebo. It is also devoid of side effects such as clinically significant hyperprolactinaemia, hypercholesterolaemia and cardiotoxicity, and has a low propensity for weight gain. Symptom relief is achieved without significant sedation. These clinical data suggest its usefulness in psychosocial rehabilitation, as well as in long-term prevention of schizophrenic relapse. Recent results from a multicentre, open-label study in a general psychiatric setting provide the first evidence that aripiprazole is also effective under naturalistic conditions. However, only post-marketing experience will show whether the positive results of these controlled trials can be replicated in everyday practice.

**SCZ & Visual scanning deficits**

- **Visual scanning deficits in schizophrenia and their relationship to executive functioning impairment.**

  **Authors:** Minassian A, Granholm E, Verney S, Perry W. Department of Psychiatry, University of California San Diego, 200 West Arbor Drive, Mailcode 8620, San Diego, CA 92103-8620, USA

  **Source:** Schizophr Res. 2005 Apr 1;74(1):69-79. Related Articles, Links

  **Summary:** Abnormal visual scanning of faces, objects, and line drawings has been observed in patients with schizophrenia and is thought to reflect neurocognitive impairment. In this study, a simultaneous measurement approach was used to assess whether schizophrenia patients demonstrate restricted visual scanning when confronted with a complex problem-solving stimulus, and whether visual scanning deficits are predictive of inflexible thinking. Thirty-eight schizophrenia patients and 30 comparison participants were presented with Rorschach inkblots while eye movements were monitored and verbal responses to the stimuli were recorded and scored for inflexible thinking using the Rorschach Repetition and Perseveration Scale. Schizophrenia patients demonstrated fewer and longer visual fixations and shorter total scanpath relative to comparison participants but did not differ on mean scanpath length. Among patients, fewer fixations were associated with a higher frequency of verbal perseverations. Correlations between scanning measures and symptoms showed that negative symptoms were related to a minimal scanning or "staring" approach. Results support previous findings of restricted visual scanning in schizophrenia patients, are consistent with previously observed relationships between visual scanning and symptom profiles, and suggest that visual organizational deficits during complex problem-solving tasks may be related to cognitive inflexibility and frontal-executive dysfunction.

**SCZ, Tyrosine kinetics & Cognitive dysfunction**

- **Kinetics of tyrosine transport and cognitive functioning in schizophrenia.**

  **Authors:** Wiesel FA, Edman G, Flyckt L, Eriksson A, Nyman H, Venizelos N, Bjerkenstedt L. - Department of Neuroscience, Psychiatry, Ulleraker, Uppsala University Hospital, Uppsala SE-750 17, Sweden

  **Source:** Schizophr Res. 2005 Apr 1;74(1):81-9. Related Articles, Links

  **Summary:** BACKGROUND: Tyrosine supplementation in humans has been shown to improve cognitive functioning. Several studies have demonstrated a decreased maximal transport capacity of tyrosine (V(max)) across the cell membrane and an increased affinity (K(m)) of tyrosine to membrane binding sites in schizophrenic patients. A lack of tyrosine for dopamine synthesis with impairment of dopaminergic transmission could impair cognitive functioning. Aberrant tyrosine kinetics in patients with schizophrenia might therefore be associated with cognitive dysfunction-a core feature of schizophrenia. METHODS: Tyrosine kinetics was determined in cultured fibroblasts from 36 schizophrenic patients. The kinetic parameters V(max) and K(m) were calculated and then the patients were divided into two groups according to the median of the kinetic parameters. A comprehensive neuropsychological test battery was used to evaluate cognitive functioning. RESULTS: Patients with low K(m) (below the median) had poorer cognitive performance than patients with high K(m) (above the median). V(max) did not discriminate schizophrenic patients with cognitive dysfunction to the same extent. Conclusions: Changes in tyrosine transport probably influence cognitive functioning via the dopamine system. However, our findings of a relation between low K(m) and cognitive dysfunction may have a more complex background. It is suggested that the connection is related to genetically determined membrane factors that disturb communication/transmission among neurons.

**SCZ & Recognition memory**

- **Levels of processing effects on recognition memory in patients with schizophrenia.**

  **Authors:** Paul BM, Elvevag B, Bokat CE, Weinberger DR, Goldberg TE. - Clinical Brain Disorders Branch, National Institute of Mental Health, 10 Center Drive, MSC 1379, Bethesda MD 20892, USA

  **Source:** Schizophr Res. 2005 Apr 1;74(1):101-10. Related Articles, Links

  **Summary:** This study sought to characterize the performance of patients with schizophrenia, as compared with healthy participants, on a memory task that required encoding of items to different depths. Participants included 21 individuals with schizophrenia and 26 healthy controls. During the encoding phase of the study, participants processed successively
results suggest that they form a more enduring characteristic of this disorder than has previously been assumed.

monitoring are a prominent feature of schizophrenia, and our cognitive domains. No relationship was found between source-performance was related to selective attention, but not to other imagined thoughts as verbalized thoughts. Source-monitoring monitoring performance, discrimination index, and response bias (n=15). On the basis of a source-monitoring task in which an internal source-monitoring task with that of normal controls may underlie positive symptoms of schizophrenia, the current tests and symptomatology questionnaires. Relative to controls, some patients, escitalopram may have use.

Bipolar depression, Risperidone & Paroxetine

Risperidone and paroxetine given singly and in combination for bipolar depression.

Authors: Shelton RC, Stahl SM. - From the Department of Psychiatry, Vanderbilt University School of Medicine, Nashville, Tenn. (Dr. Shelton); and Neuroscience Education Institute, Carlsbad, Calif. (Dr. Stahl)


Summary: Background: Bipolar depression is a major clinical problem that remains under-researched. The current study was intended to evaluate the effects of the novel antipsychotic risperidone, the selective serotonin reuptake inhibitor (SSRI) for adolescents is fluoxetine. However, in clinical practice all antidepressants are used in adolescents. Five patients had parents who opted for the use of escitalopram instead of other treatments. Reasons included poor response and side effects from other SSRIs. Specifically, escitalopram was considered possibly less likely to cause obesity than paroxetine. It also caused a lower frequency of akathisia than fluoxetine, more stable blood levels over years than sertraline, very low drug interactions, and a low onset of anxiety if using a 5-mg starting dose. Although studies in adolescents are very limited for escitalopram, its parent medication - citalopram – has been used in over 40 million patients. Parents and adolescent patients should be made aware of all antidepressant options, if psychopharmacology is indicated. In some patients, escitalopram may have use.

Confusing thoughts and speech

Confusing thoughts and speech: source monitoring and psychosis.

Authors: Henquet C, Krabbendam L, Dautzenberg J, Jolles J, Merckelbach H. - Department of Psychiatry and Neuropsychology, South Limburg Mental Health Research and Teaching Network, EURON, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

Source: Psychiatry Res. 2005 Jan 30;133(1):57-63. Related Articles, Links

Summary: To explore the idea that deficits in source monitoring may underlie positive symptoms of schizophrenia, the current study compared schizophrenic patients’ performance (n=15) on an internal source-monitoring task with that of normal controls (n=15). On the basis of a source-monitoring task in which participants had to recall whether they had verbalized answers or merely thought about these answers, overall source monitoring performance, discrimination index, and response bias were calculated. In addition, participants completed cognitive tests and symptomatology questionnaires. Relative to controls, patients had significantly more difficulties with monitoring their own actions and showed a tendency towards misclassifying imagined thoughts as verbalized thoughts. Source-monitoring performance was related to selective attention, but not to other cognitive domains. No relationship was found between source-monitoring and symptomatology. Failures in internal source monitoring are a prominent feature of schizophrenia, and our results suggest that they form a more enduring characteristic of this disorder than has previously been assumed.

Escitalopram in Adolescent Major Depression

Authors: James L. Schaller, MD, PA; David B. Rawlings, PhD, PA

Summary: Escitalopram is the purified functional isomer contained in citalopram. Escitalopram is now prescribed in 26 countries. In the United States, the only US Food and Drug Administration (FDA)-approved selective serotonin reuptake inhibitor (SSRI) for adolescents is fluoxetine. However, in clinical practice all antidepressants are used in adolescents. Five patients had parents who opted for the use of escitalopram instead of other treatments. Reasons included poor response and side effects from other SSRIs. Specifically, escitalopram was considered possibly less likely to cause obesity than paroxetine. It also caused a lower frequency of akathisia than fluoxetine, more stable blood levels over years than sertraline, very low drug interactions, and a low onset of anxiety if using a 5-mg starting dose. Although studies in adolescents are very limited for escitalopram, its parent medication - citalopram – has been used in over 40 million patients. Parents and adolescent patients should be made aware of all antidepressant options, if psychopharmacology is indicated. In some patients, escitalopram may have use.

MDD, Adolescent & Escitalopram

Escitalopram in Adolescent Major Depression

Authors: James L. Schaller, MD, PA; David B. Rawlings, PhD, PA

Summary: Escitalopram is the purified functional isomer contained in citalopram. Escitalopram is now prescribed in 26 countries. In the United States, the only US Food and Drug Administration (FDA)-approved selective serotonin reuptake inhibitor (SSRI) for adolescents is fluoxetine. However, in clinical practice all antidepressants are used in adolescents. Five patients had parents who opted for the use of escitalopram instead of other treatments. Reasons included poor response and side effects from other SSRIs. Specifically, escitalopram was considered possibly less likely to cause obesity than paroxetine. It also caused a lower frequency of akathisia than fluoxetine, more stable blood levels over years than sertraline, very low drug interactions, and a low onset of anxiety if using a 5-mg starting dose. Although studies in adolescents are very limited for escitalopram, its parent medication - citalopram – has been used in over 40 million patients. Parents and adolescent patients should be made aware of all antidepressant options, if psychopharmacology is indicated. In some patients, escitalopram may have use.
who treat patients with depression are all too familiar with those who do not seem to respond to antidepressants or who respond for a while and then relapse. According to Verinder Sharma, MB, FRCP(C), many of these patients probably have bipolar disorder. Dr. Sharma is a psychiatrist at the Mood Disorders Program of St. Joseph's Health Care and a professor of psychiatry at the University of Western Ontario in London, Ontario, Canada. He presented his research into misdiagnosed bipolar disorder here at the 54th annual meeting of the Canadian Psychiatric Association.

Depressed patients with bipolar features are both less likely to respond to antidepressants and more likely to have tolerability problems with these drugs, possibly because they elicit hypomanic symptoms such as agitation and sleep disturbance, said Dr. Sharma. What is less known is whether these bipolar features are subtle enough for clinicians to miss them if they are not careful.

"There are a lot of diagnoses for which we really have to do better screening," Dr. Sharma told Medscape. "What is happening is sometimes people overemphasize the issue of cross-sectional symptoms, whereas with mood disorders, we really have to look at people over a period of time in order to know what we're dealing [with]. So, [for] some of these people, it's possible that at some point they were clearly unipolar, but when we observe them over a period of time, it's more clear [that they have bipolar features]."

In addition to poor response to antidepressants, signs that seemingly depressed patients may have bipolar disorder include an early age of onset, the presence of multiple episodes over a long period of time, a family history of bipolar disorder, a history of postpartum depression, a history of psychotic symptoms, and a hyperthymic personality when not depressed.

One challenge is the changing definition of bipolarity. "What we have seen over the past few years is the expansion of the bipolar spectrum," said Dr. Sharma. It may be helpful to look at unipolar depression and bipolar disorder as separate entities of a continuum, rather than distinct diseases, he added.

Dr. Sharma and colleagues used the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) to reinterview 61 patients diagnosed with unipolar depression who had failed to respond to at least two adequate courses of antidepressants. By examining their symptoms over time as well as their family history, the researchers discovered that 35% of these patients had a form of bipolar disorder. Even more remarkably, after following them for a year, fully 80% of patients were deemed to have bipolar disorder.

"In a large number of these patients, we were able to stop antidepressants and to treat them with mood stabilizers, usually in combination with neuroleptics," said Dr. Sharma during his presentation. Specifically, 93% of patients were taking antidepressants at intake compared with 34% after one year of follow-up. The other 66% were taking mood stabilizers, often combined with atypical neuroleptics. Many of those who remained on antidepressant therapy had been switched to monoamine oxidase inhibitors.

"We urge caution about the use of antidepressants in patients who have a history of loss of response because, in these patients, some of them developed treatment-refractory symptoms because of the overuse or misuse of antidepressants," Dr. Sharma said during his presentation. "There may be a subgroup of people in whom we may be contributing to treatment refractoriness by giving them antidepressants," Dr. Sharma told Medscape. "In these people, you really have to be using mood stabilizers."

**LTG & Preventing Depressive —**

*Lamotrigine Is Helpful in Preventing Depressive Relapses in Bipolar Disorder*

**Authors:** Laure B. W. MD

**Source:** ICBP 2004: Abstract 5. February 9-13, 2004. Reviewed by Gary D. Vogen, MD

**Summary:** Feb. 18, 2004 — Lamotrigine (LTG) is better than placebo or lithium for preventing depressive relapses in bipolar disorder, according to a presentation at the International Congress of Biological Psychiatry held in Sydney, Australia, from Feb. 9-13. The results of this study suggest that [LTG] is the only medication that has better efficacy in preventing depressive relapse, lead author Lakshmi N. Yatham, MBBS, FRCP, MRCPsych, told Medscape. Dr. Yatham is a professor of psychiatry and Michael Smith Foundation Senior Scholar at the University of British Columbia in Vancouver, Canada. This has important clinical implications, as all medications currently used for prophylaxis of bipolar disorder have better efficacy in preventing mania than depression.

Lithium, which is commonly used to treat bipolar mania, is also thought to have antidepressant activity. Based on the results of two clinical trials in bipolar I disorder that enrolled 463 currently or recently depressed patients and 175 currently or recently manic patients, the investigators compared the effects of 18 months of prophylactic treatment with placebo (PBO), lithium (Li), and LTG. Compared with placebo, LTG treatment resulted in fewer recently manic patients who required intervention for depression (LTG 14%, Li 22%, PBO 30%; P = .034 for LTG vs. PBO); reported depressive adverse events (LTG 0%, Li 4%, PBO 3%); met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), criteria for depression (LTG 10%, Li 17%, PBO 28%; P = .024 for LTG vs. PBO), and had Hamilton Depression Rating Scale (HAMD) scores greater than 20 (LTG 3%, Li 11%, PBO 19%; P = .011 for LTG vs. PBO). In recently depressed patients, the treatment groups did not differ significantly in the incidence of depressive symptoms.

Intervention for depression was required in 39% of the PBO group, 34% of the LTG group, and 39% of the Li group. The corresponding proportions for reported depressive adverse events were 2%, 4%, and 3%; for DSM-IV depression, the proportions were 36%, 31%, and 36%; and for HAMD scores greater than 20 were 26%, 22%, and 18%, respectively.

The authors suggest that because LTG can protect against depressive symptoms in currently or recently manic patients, administration of LTG should be considered during or shortly after stabilization of mania, before depressive symptoms occur. "Clinicians can combine lamotrigine with lithium or atypical antipsychotics for achieving optimal control of both depression and mania."

**BD & Levetiracetam —**

*Levetiracetam Shows Promise in Treating Moderate Bipolar Disorder*

**Authors:** Jill Taylor

**Source:** 56th APA-IPS: Poster 106. Presented Oct. 8, 2004. Reviewed by Gary D. Vogen, MD

**Summary:** Oct. 11, 2004 (Atlanta) — Levetiracetam (Keppra) may be an effective and safer alternative to existing drugs in the first-line treatment of moderate bipolar disorder, suggests a study presented here at the American Psychiatric Association 56th Institute on Psychiatric Services. Bipolar disorder affects an estimated 10 million Americans and is often accompanied...
by conditions such as anxiety disorders, substance or alcohol abuse, and attention deficit hyperactivity disorder, leading many patients to require concurrent medications. Lead investigator Daniel A. Deutschman, MD, chief of psychiatry at Southwest General Health Center in Cleveland, Ohio, said that anticonvulsants are a common treatment for patients with bipolar disorder, but most carry a large burden in terms of adverse effects. The favorable safety profile of levetiracetam made the drug attractive for investigation in bipolar patients. “We were excited about this molecule, and we gave it to patients in cases where we suspected it might be better than anything else we had to offer them,” Dr. Deutschman told Medscape. "We wouldn't have to worry about liver damage or bone marrow issues, we wouldn't have to monitor sodium, and we wouldn't be causing the weight gain associated with most of the traditional medications.” A total of 109 study subjects were drawn retrospectively from a private practice. Of them, 45% were diagnosed as bipolar II, 37% as bipolar II subsyndromal, and 18% as bipolar I. Half of the subjects were men, the median age was 30 years (range, 6-69 years), and the median duration of treatment with levetiracetam was 76 days (range, 14 days to one year) at an average dose of 1,838 mg per day (range, 125 – 5,250 mg/day). Response to treatment was assessed retrospectively using electronic medical records, and symptom severity was tracked on a Likert scale. Analysis was performed in SAS and Systat, and symptom improvement was tested using t tests (overall change) and McNemar's test (individual symptoms). Results showed that overall symptom severity improved significantly in patients (t = 3.77; P < .001). Common individual symptoms, including irritability, racing thoughts, mood swings, and extra energy, also showed significant improvement (P < .01) when separately analyzed. In addition, adherence was observed to be high, with 8% of subjects discontinuing the medication. Adverse effects were reported by 19% of patients, with the most common being mild sedation. Three percent of patients discontinued treatment as a direct result of adverse effects. According to Dr. Deutschman, the study is limited by the fact that it is retrospective and does not benefit from randomization and blind evaluation. However, he noted that the strength of the study lies in complex and diverse "real-world" patients, making the results easy to generalize to practicing physicians. Dr. Deutschman also noted that this treatment option is not suitable for patients experiencing severe mania, primarily due to dosing requirements that can vary widely between individuals.

**Costs, Bipolar depression & Mania**

*The Economic Burden of Bipolar-Related Phases of Depression Versus Mania*

**Authors:** Alex Z. Fu, MS; Anu A. Krishnan, MS; Sonya D. Harris, MPH; Thomas R. Thompson, MD

**Summary:** Health care resource utilization and costs of bipolar depression compared with costs of bipolar mania were determined retrospectively using data from 1998 to 2002 obtained from a national managed care claims database. Medical claims and health care events were characterized as depressive or manic using International Classification of Diseases, Ninth Revision codes. Costs were compared using t tests and multivariate linear regression. Depressive episodes occurred 3 times as often as manic episodes in persons with a diagnosis of bipolar disorder. Annual bipolar depression-related outpatient and inpatient costs were 4 and 2 times higher, respectively, than costs related to mania. Estimated costs of a depressive episode and a manic episode were $5503 and $2842, respectively. In this sample, bipolar-related depressive episodes predominated, used more health care resources, and cost more than manic episodes.

**Introduction:** Bipolar disorder, a common, serious, psychiatric condition characterized by recurrent episodes of depression and hypomania or mania, with intervening periods of euthymia, is a major cause of disability worldwide. The Global Burden of Disease Study, conducted by the World Health Organization, ranked bipolar affective disorder second among mental illnesses and sixth among the leading causes of worldwide disability in persons aged 15 to 44 years.[1] Bipolar disorder has a significant impact on psychosocial and vocational functioning and quality of life. Persons with bipolar disorder have substantially lower health-related quality of life and functionality compared with the general population,[2-4] which results in increased medical and work-impairment costs[5] and poor long-term outcomes.[4]

Of the 2 affective states, depression predominates and is more debilitating than mania.[5,6] Patients with bipolar disorder experience depressive symptoms 3 times more often than manic symptoms,[6] causing greater disruption than manic symptoms to careers, family, and social functioning.[7] Among patients with bipolar disorder, depressive symptoms have been identified as the most significant contributor to subsequent morbidity and poor function.[8-10] In addition, recovery from depression is slower and less complete than recovery from mania. A comparative study of recovery rates for manic and depressive episodes found that 46% of manic versus 36% of depressive episodes abated at 1 month, 64% versus 44% at 2 months, and 93% versus 78% at 18 months.[11] Moreover, the relative risk of suicide during bipolar-related depressive episodes is 30 times greater than the risk during manic episodes.[12]

Bipolar disorder is the second most costly mental illness, exceeded only by schizophrenia.[13] Total annual costs of bipolar disorder have been reported to range from $24 billion to $45.2 billion.[14,15] However, the costs of the depressive phase relative to the manic phase has not been systematically examined. In this study, we analyzed health care resource utilization and the economic burden of bipolar depression versus mania using medical claims data from a national managed care claims database that compiled information from more than 30 managed care health plans operating in the United States.

**Testosterone, Hypogonadal men & MDD**

*Safety and efficacy of testosterone gel 1% augmentation in depressed men with partial response to antidepressant therapy.*

**Authors:** Orego CA, Fullerton L, Kunik ME. - Veterans Affairs Medical Center, Houston, TX, Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, Veterans Affairs South Central Mental Illness Research, Education, and Clinical Center (MIRECC)


**Related Articles, Links**

**Summary:** The current study evaluates the efficacy and safety of testosterone (T) gel 1% augmentation on depressive symptoms and quality of life in treatment-resistant, depressed, hypogonadal men older than 50 years of age who are receiving antidepressants. The authors hypothesized that T augmentation...
would improve depressive symptoms and quality of life. Eighteen hypogonadal men entered the study who had had an adequate trial of antidepressant therapy and had significant depressive symptoms. Participants were continued on their antidepressant and were randomized to receive either placebo or active T gel (5 g) to be applied once a day. Participants were tested on 6 occasions: screening visit, an initial session (pretreatment), at 6 and 12 weeks during the first treatment condition, and at 18 and 24 weeks during the crossover condition. The authors found a significant improvement in depressive symptoms from baseline to 12 weeks of testosterone treatment. However, a statistical difference between placebo and testosterone treatment phases was not demonstrated. The limitations of the study, including the chronicity and severity of patients’ depression, variability in T levels, and a small sample size, probably influenced the ability to detect a discernable difference. Nevertheless, the study shows that T gel augmentation may be helpful in hypogonadal males with depression.

**DPD, Comorbidity & PDs**

**Depressive personality disorder:** rates of comorbidity with personality disorders and relations to the Five-Factor Model of Personality.

**Authors:** Bagby RM, Schuller DR, Marshall MB, Ryder AG. Centre for Addiction and Mental Health, and Department of Psychiatry, University of Toronto, Ontario, Canada. michael_bagby@camh.net

**Source:** J Personal Disord. 2004 Dec;18(6):542-54. Related Articles, Links

**Summary:** Depressive personality disorder (DPD) is listed in the DSM-IV as one of the "Disorders for Further Study." In this investigation we examined (1) the rates of comorbidity of DPD with the 10 personality disorders (PDs) in the main text of DSM-IV, and (2) the convergent and discriminant validity of DPD in its relation to the 30 facet traits of the Five-Factor Model of personality (FFM). One hundred and sixty-nine participants with psychiatric diagnoses were interviewed with the Structured Clinical Interview for DSM-IV Personality Disorders Questionnaire (SCID-II) and completed the Revised NEO Personality Inventory (NEO PI-R). A total of 26 (15%) of the participants met diagnostic criteria for at least one of the 10 main text PDs, and 15 (9%) met criteria for DPD. Of those who met criteria for DPD, 10 (55%) of the participants also met criteria for one or more of the 10 main text PDs. Regression analyses indicated a four-facet trait set derived from the NEO PI-R thought to be uniquely associated with DPD accounted for a significant amount of variance in DPD SCID-II PD scores and was significantly larger for DPD than it was for the 9 of the 10 main text PDs: the sole exception was for avoidant PD. Diagnostically, DPD overlaps significantly with other PDs but is distinguishable in its unique relation with traits from the FFM.

**UD, Bupropion & Venlafaxine**

**Bupropion and venlafaxine responders differ in pretreatment regional cerebral metabolism in unipolar depression.**

**Authors:** Little JT, Ketter TA, Kimbrell TA, Dunn RT, Benson BE, Willis MW, Luckenbaugh DA, Post RM. - Division of Psychiatric Neuroimaging, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland; Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, Maryland

**Source:** Biol Psychiatry. 2005 Feb 1;57(3):220-8. Related Articles, Links

**Summary:** BACKGROUND: Pretreatment functional brain imaging was examined for never-hospitalized outpatients with unipolar depression compared with control subjects in a crossover treatment trial involving bupropion or venlafaxine monotherapy. METHODS: Patients (n = 20) with unipolar depression received baseline (medication-free) fluoxetine-18 deoxyglucose (FDG) positron emission tomography (PET) scan and then at least 6 weeks of bupropion or venlafaxine monotherapy in a single-blind crossover trial. Age-matched healthy control subjects (n = 20) also received baseline FDG PET scans. For each medication PET data from patients compared with control subjects was analyzed as a function of treatment response (defined as moderate to marked improvement on the Clinical Global Impression Scale). RESULTS: Treatment response rates were similar for bupropion (32%) and venlafaxine (33%). Compared with control subjects, responders but not nonresponders, to both drugs demonstrated frontal and left temporal hypometabolism. Selectively, compared with control subjects bupropion responders (n = 6) also had cerebellar hypermetabolism, whereas venlafaxine responders (n = 7) showed bilateral temporal and basal ganglia hypometabolism. Conclusions: These data suggest that pretreatment frontal and left temporal hypometabolism in never-hospitalized depressed outpatients compared with control subjects is linked to positive antidepressant response and that additional alterations in regional metabolism may be linked to differential responsivity to bupropion and venlafaxine monotherapy.

**DHEA & Midlife – onset depression**

**DHEA and midlife major and minor depression.**

**Authors:** Schmidt PJ, Daly RC, Bloch M, Smith MJ, Danaceau MA, St Clair LS, Murphy JH, Haq N, Rubinow DR. - Behavioral Endocrinology Branch, National Institute of Mental Health, Rockville, MD 20892-1276, USA. Peter.Schmidt@mail.nih.gov

**Source:** Arch Gen Psychiatry. 2005 Feb;62(2):154-62. Related Articles, Links

**Summary:** CONTEXT: Alternative and over-the-counter medicines have become increasingly popular choices for many patients who prefer not to take traditional antidepressants. The adrenal androgen and neurosteroid dehydroepiandrosterone (DHEA) is available as over-the-counter hormonal therapy and previously has been reported to have antidepressant-like effects. OBJECTIVE: To evaluate the efficacy of DHEA as a monotherapy treatment for midlife-onset depression. DESIGN: A double-blind, randomized, placebo-controlled, crossover treatment study was performed from January 4, 1996, through August 31, 2002. Settings: The National Institute of Mental Health Midlife Outpatient Clinic in the National Institutes of Health Clinical Center, Bethesda, Md. Patients: Men (n = 23) and women (n = 23) aged 45 to 65 years with midlife-onset major or minor depression participated in this study. None of the subjects received concurrent antidepressant medications. Intervention: Six weeks of DHEA therapy, 90 mg/d for 3 weeks and 450 mg/d for 3 weeks, and 6 weeks of placebo. MAIN OUTCOME MEASURES: The 17-item Hamilton Depression Rating Scale and Center for Epidemiologic Studies Depression Scale.
Additional measures included the Derogatis Interview for Sexual Functioning. Results were analyzed by means of repeated-measures analysis of variance and post hoc Bonferroni t tests. RESULTS: Six weeks of DHEA administration was associated with a significant improvement in the 17-Item Hamilton Depression Rating Scale and the Center for Epidemiologic Studies Depression Scale ratings compared with both baseline (P<0.01) and 6 weeks of placebo treatment (P<0.01). A 50% or greater reduction in baseline Hamilton Depression Rating Scale scores was observed in 23 subjects after DHEA and in 13 subjects after placebo treatments. Six weeks of DHEA treatment also was associated with significant improvements in Derogatis Interview for Sexual Functioning scores relative to baseline and placebo conditions. Conclusion: We find DHEA to be an effective treatment for midlife-onset major and minor depression.

**Topiramate, Risperidone & Acute Mania**

- **Topiramate and divalproex in combination with risperidone for acute mania: a randomized open-label study.**

  **Authors:** Bahk WM, Shin YC, Woo JM, Yoon BH, Lee JS, Jon Di, Chung SK, Choi SK, Paik IH, Pae CU. - Department of Psychiatry, St. Mary's Hospital, The Catholic University of Korea College of Medicine, Seoul, South Korea


  **Summary:** Mood stabilizers and atypical antipsychotics are commonly combined for the treatment of bipolar mania. The aim of this study was to compare the effectiveness and tolerability of topiramate and divalproex in combination with risperidone for treating acute mania patients in a naturalistic treatment setting. Seventy-four patients who met the DSM-IV criteria for bipolar mania enrolled in this study. In order to assess the efficacy and the extrapyramidal symptoms (EPS), the Young Mania Rating Scale (YMRS), Clinical Global Impression (CGI) and Simpson-Angus Rating Scale (SARS) were measured at the baseline and at weeks 1, 3 and 6. From the baseline to the endpoint, the YMRS and CGI scores were reduced by 67.9% and 63.7% in the divalproex plus risperidone group (TPMG). The YMRS and CGI scores were also reduced by 63.7% and 58.2% in the divalproex and risperidone group (DVPD). The weight and body mass index (BMI) increased significantly by 58.2% in the divalproex plus risperidone group (TPMG). The YMRS and CGI scores were also reduced by 63.7% and 58.2% in the divalproex and risperidone group (DVPD).

  **MDD, Probiotics & Adjuvant therapy**

  - **Major depressive disorder: probiotics may be an adjuvant therapy.**

    **Authors:** Logan AC, Katzman M. - Nutrition Research Consulting, 50 Yonkers Terrace, 8-J Yonkers, NY 10704, USA

    **Source:** Med Hypotheses. 2005;64(3):533-8. Related Articles, Links

    **Summary:** Major depressive disorder (MDD) is an extremely complex and heterogeneous condition. Emerging research suggests that nutritional influences on MDD are currently underestimated. MDD patients have been shown to have elevated levels of pro-inflammatory cytokines, increased oxidative stress, altered gastrointestinal (GI) function, and lowered micronutrient and omega-3 fatty acid status. Small intestinal bacterial overgrowth (SIBO) is likely contributing to the limited nutrient absorption in MDD. Stress, a significant factor in MDD, is known to alter GI microflora, lowering levels of lactobacilli and bifidobacterium. Research suggests that bacteria in the GI tract can communicate with the central nervous system, even in the absence of an immune response. Probiotics have the potential to lower systemic inflammatory cytokines, decrease oxidative stress, improve nutritional status, and correct SIBO. The effect of probiotics on systemic inflammatory cytokines and oxidative stress may ultimately lead to increased brain derived neurotrophic factor (BDNF). It is our contention that probiotics may be an adjuvant to standard care in MDD.

  **BPD, Impulsivity & Aggression**

  - **The relationship between impulsivity, aggression, and impulsive-aggression in borderline personality disorder: an empirical analysis of self-report measures.**

    **Authors:** Critchfield KL, Levy KN, Clarkin JF. - New York Presbyterian Hospital, Joan and Sanford I. Weill Cornell Medical College, USA. psykcl@psych.utah.edu

    **Source:** J Personal Disord. 2004 Dec;18(6):555-70. Related Articles, Links

    **Summary:** Impulsivity has been repeatedly identified as a key construct in BPD; however, its precise definition seems to vary especially regarding the overlap with aggression. The term impulsive-aggression, also generally seen as central to an understanding of BPD, seems to address itself to the interface between the two, but has itself been used inconsistently in the literature, sometimes having reference to a unitary phenotypic dimension, and at other times suggesting some combination of distinct traits. This study examined the relationship between multiple measures of impulsivity, aggression, and impulsive-aggression in a BPD sample (N = 92) in order to clarify the relationship between these measured constructs in this clinical population. Results show little relationship between measures of aggression and impulsivity in BPD, with measures of impulsive-aggression correlating strongly with measures of aggression only. Implications of the present results for future research and clinical work with BPD are discussed.

  **ATD method, Mood & Cognitive disturbances**

  - **Effects of a novel method of acute tryptophan depletion on plasma tryptophan and cognitive performance in healthy volunteers.**

    **Authors:** Evers EA, Tillie DE, van der Veen FM, Lieben CK, Jolles J, Deutz NE, Schmitt JA. - Department of Psychiatry and Neuropsychology (DRT10), Brain and Behavior Institute, Maastricht University, P.O. Box 616, Maastricht, 6200, The Netherlands, l.evers@np.unimaas.nl

    **Source:** Psychopharmacology (Berl). 2004 Dec 23; [Epub ahead of print] Related Articles, Links

    **Summary:** RATIONALE: Disorders associated with low levels of serotonin (5-HT) are characterized by mood and cognitive disturbances. Acute tryptophan depletion (ATD) is an established method for lowering 5-HT levels and an important tool to study the effects of reduced 5-HT on mood and cognition in human subjects. The traditional ATD method, i.e., administration of separate amino acids (AAs), has several
disadvantages. The AA mixture is costly, unpalatable and associated with gastrointestinal discomfort. OBJECTIVES: The University of Maastricht developed a new and inexpensive method for ATD: a natural collagen protein (CP) mixture with low tryptophan (TRP) content. The reductions in plasma TRP after taking this CP mixture were compared with the reductions achieved taking the traditional AA mixture, and effects on memory and reversal learning were studied. METHODS: Fifteen healthy young volunteers participated in a double-blind, counterbalanced within-subject study. Reversal learning, verbal memory and pattern recognition were assessed at baseline and 3-4 h after taking the CP mixture. RESULTS: The new ATD method significantly reduced plasma TRP by 74% and the ratio between TRP and the other large AAs (TRP/LNAA) by 82%. The placebo mixture did not change these measures. Delayed recognition reaction time on the verbal learning task was increased following ATD. No other cognitive effects were found. CONCLUSIONS: The CP mixture was shown to be an efficient tool for lowering plasma TRP in humans. The validity of this method with regard to behavioral changes remains to be established in healthy, vulnerable and clinical populations.

**Hippocampus, Amygdala & MDD**

*Anatomical MRI study of hippocampus and amygdala in patients with current and remitted major depression.*

**Authors:** Caetano SC, Hatch JP, Brambilla P, Sassi RB, Nicoletti M, Malinger AG, Frank E, Kupfer DJ, Keshavan MS, Severe JC. - Division of Mood and Anxiety Disorders, Department of Psychiatry, University of Texas Health Sciences Center at San Antonio, TX, USA.

**Source:** Psychiatry Res. 2004 Dec 15;132(2):141-7. Related Articles, Links

**Summary:** Morphometric MRI studies suggest decreased hippocampal volumes in currently depressed patients, with conflicting findings for the amygdala. We studied these temporal lobe structures and superior temporal gyrus (STG) in patients with current and remitted major depression. We scanned 31 unmedicated depressed patients (21 currently depressed, 10 remitted) and 31 matched healthy controls with a 3D SPGR sequence in a 1.5 Tesla GE Signa Imaging System. There was a trend towards smaller left amygdala volumes in all depressed patients compared with healthy controls. We found significantly smaller hippocampal volumes bilaterally in currently depressed patients than in remitted patients. Furthermore, we found a statistically significant inverse correlation between length of illness and left hippocampus volumes and right superior temporal gyrus volumes. Our finding of smaller hippocampi in currently depressed patients is consistent with the hypothesis that hypercortisolism could result in hippocampal neurotoxicity in major depression. A smaller hippocampal size may be more characteristic of the depressive state and not be present in remitted patients.

**Serotonergic function & Affective states**

*Serotonergic function in the central nervous system is associated with daily ratings of positive mood.*

**Authors:** Flory JD, Manuck SB, Matthews KA, Muldoon MF. - Department of Psychology, University of Pittsburgh, 4015 O’Hara Street, Pittsburgh, PA 15260, USA.

**Source:** Psychiatry Res. 2004 Nov 30;129(1):11-9. Related Articles, Links

**Summary:** Serotonin constrains a broad array of animal and human behavior and may also inhibit the expression of mood or affective states among humans. For the most part, this research has focused on the association of central serotonergic function with negative affectivity (i.e., anxiety, depression, hostility), with less attention on the relationship between serotonergic function and positive affect or mood. The current study was conducted to examine the relationship between a measure of central serotonergic activity and daily ratings of positive and negative mood in a nonpatient sample. Two hundred and fifty-four adults, aged 24-60, completed end-of-day ratings of positive and negative mood items over 7 consecutive days. A neuropharmacological challenge was administered to index central serotonergic function, i.e., the maximal prolactin (PRL) response to fenfluramine, a serotonin releasing agent. Hierarchical linear regression analyses indicated that the peak PRL response to fenfluramine was positively associated with positive mood, averaged over 7 days, after controlling for known predictors of the PRL response. This relationship remained significant after controlling for average negative mood, for the presence of a current DSM-III-R diagnosis, and for trait measures of Neuroticism and Extraversion. In contrast, the PRL response to fenfluramine was not associated with average negative mood, although it was inversely correlated with trait negative affectivity (i.e., Neuroticism). These results suggest that deficiencies in serotonergic function may reflect the relative absence of positive mood.

**AN & Depression syndromes**

*(Depression syndromes in patients suffering from anorexia nervosa) [Article in Polish]*

**Authors:** Lucka I. - Kliniki Psychiatrii Rozwojowej, Zaburzen Psychotycznych i Wieku Podeszlego AM w Gdansku


**Summary:** AIM: The purpose of the study was the estimation of comorbidity of depressive syndromes and anorexia nervosa (based on criteria of ICD-10 and DSM-IV). A group of 30 children (average age–13.5), 27 girls and 3 boys suffering from a first episode of anorexia nervosa was considered. METHOD: Anamnesis from patients and their parents, clinical observation, the psychiatric investigation with use of The Depression Rating Scale for Children (Elva o. Poznanski and comp.) and the Hamilton Depression Rating Scale. RESULTS: The comorbidity of depressive syndromes and anorexia nervosa was frequently observed. 73.3% children suffered from depressive syndromes in the course of anorexia nervosa. As for intensity—in 33% it was moderate, in 20%–severe, and in 20%—mild depression. In the investigated group of children depressive syndromes appeared in the bulimic subtype of anorexia nervosa in 88.8% cases and in the restricting subtype in 72.2%. Statistically, in the considered group, the depression was significantly frequent in the first and the second degree relatives. CONCLUSIONS: In the examined group, the number of biological as well as psychological events which could predispose to depression was found. However, the children were not suffering from depression until they were sick from anorexia nervosa and their bodies were not cachectic.
**Trazodone, Venlafaxine & MDD**

- **Trazodone addition for insomnia in venlafaxine-treated, depressed inpatients: a semi-naturalistic study.**

  **Authors:** Bertschy G, Ragama-Pardos E, Muscionico M, Alt-Ameur A, Roth L, Osiek C, Ferrero F. - Department of Psychiatry, University Hospital and University of Geneva, Geneva, Switzerland. gilles.bertschy@hcuge.ch

  **Source:** Pharmacol Res. 2005 Jan;51(1):79-84. Related Articles, Links

  **Summary:** In this paper, we present the results of a prospective semi-naturalistic study of the addition of trazodone for insomnia to a 4 week, 300mg/day venlafaxine treatment in 50 depressed inpatients. The Montgomery and Asberg depression rating scale was used as a rating instrument. The study is designated as semi-naturalistic due to the fact that, although the venlafaxine treatment regimen was strictly defined, the timing of the trazodone introduction and the dosage were determined by the clinicians.

  The indication was based on the persistency of insomnia despite the use of authorized sedative co-medication (zopiclone as a hypnotic, clorazepate as an anxiolytic). Among the 42 patients who completed the study, 27 did not receive trazodone (G1) while 15 did (G2). Although the two groups were not clinically different at study entry, G2 patients showed less improvement than G1 patients during venlafaxine treatment alone, both in terms of insomnia (MADRS item 4) and inner tension (MADRS item 3). After trazodone introduction, insomnia improved and the median (interquartile range) of this item in G1 and G2 patients showed no statistically significant difference on Day 28 (G1: 0 (0-1); G2: 0 (0-2)). However, inner tension did not improve and the median (interquartile range) was higher on Day 28 in G2 patients (G1: 1 (0-2); G2: 2 (1-4); P < 0.05). Thus, trazodone is probably used for patients who develop not only insomnia, but also other tension/anxiety during venlafaxine treatment. However, it alleviates only the first symptom, not the second.

**SAMe & Depression with HIV/AIDS**

- **S-adenosylmethionine (SAM-e) for the treatment of depression in people living with HIV/AIDS.**

  **Authors:** Shippy RA, Mendez D, Jones K, Cergnul I, Karpik SE. - ACRIA (AIDS Community Research Initiative of America), 230 West 38th St, 17th Floor, New York, NY 10018, USA. ashippy@acria.org

  **Source:** BMC Psychiatry. 2004 Nov 11;4(1):38. Related Articles, Links

  **Summary:** BACKGROUND: This study reports on clinical data from an 8-week open-label study of 20 HIV-seropositive individuals, diagnosed with Major Depressive Disorder (DSM-IV), who were treated with SAM-e (S-Adenosylmethionine). SAM-e may be a treatment alternative for the management of depression in a population reluctant to add another "pill" or another set of related side effects to an already complex highly active antiretroviral therapy (HAART) regimen. METHODS: The Hamilton Rating Scale for Depression (HAM-D) and the Beck Depression Inventory (BDI) were used to assess depressive symptomatology from 1, 2, 4, 6 and 8 weeks after initiation of treatment with SAM-e. RESULTS: Data show a significant acute reduction in depressive symptomatology, as measured by both the HAM-D and the BDI instruments. **Conclusions:** SAM-e has a rapid effect evident as soon as week 1 (p < .001), with progressive decreases in depression symptom rating scores throughout the 8 week study.

**MDD & 5-HTTLPR**

- **The power of sample size and homogenous sampling: Association between the 5-HTTLPR serotonin transporter polymorphism and major depressive disorder.**


  **Source:** Biol Psychiatry. 2005 Feb 1;57(3):247-51. Related Articles, Links

  **Summary:** BACKGROUND: Several lines of evidence indicate that abnormalities in the functioning of the central serotonergic system are involved in the pathogenesis of affective illness. A 44-base-pair insertion/deletion polymorphism in the 5′ regulatory region of the serotonin transporter gene (5-HTTLPR), which influences expression of the serotonin transporter, has been the focus of intensive research since an initial report on an association between 5-HTTLPR and depression-related personality traits. Consistently replicated evidence for an involvement of this polymorphism in the etiology of mood disorders, particularly in major depressive disorder (MDD), remains scant. METHODS: We assessed a potential association between 5-HTTLPR and MDD, using the largest reported sample to date (466 patients, 836 control subjects). Individuals were all of German descent. Patients were systematically recruited from consecutive inpatient admissions. Control subjects were drawn from random lists of the local Census Bureau and screened for psychiatric disorders. RESULTS: The short allele of 5-HTTLPR was significantly more frequent in patients than in control subjects (45.5% vs. 39.9%; p = .006; odds ratio = 1.26). **Conclusions:** These results support an involvement of 5-HTTLPR in the etiology of MDD. They also demonstrate that the detection of small genetic effects requires very large and homogenous samples.

**BD & Maintenance treatment**

- **Treatment options for bipolar depression.**

  **Authors:** Bowden CL. - From the Department of Psychiatry, University of Texas Health Science Center, San Antonio


  **Summary:** Bipolar disorder is often misdiagnosed as major depressive disorder because of the high frequency of depressive symptomatology in many patients with bipolar disorder. Depressive episodes that are resistant to treatment may also be associated with a worse course of illness in bipolar disorder, but we do not yet understand all the factors in the connection between bipolar disorder and depression. The data on the effectiveness of antidepressants in the treatment of depression in bipolar disorder vary greatly, and there have been few prospective, randomized studies on the subject. From the data so far, the rates of induction of mania for selective serotonin reuptake inhibitors and lamotrigine seem similar to those seen with placebo. The optimal length of time to continue antidepressant treatment in patients with bipolar disorder has
not yet been determined; however, research tends to indicate that a longer term of treatment (6 months or more) may aid in the prevention of relapse. Newer U.S. Food and Drug Administration-approved treatments for depression in bipolar disorder include a combination of olanzapine and fluoxetine, which is used for depressive episodes in bipolar disorder, and lamotrigine, which is used for maintenance treatment of bipolar I disorder. Psychoeducation has also been examined as a possible treatment for depression in bipolar disorder, and a study has shown that patients receiving psychoeducation plus medication may have a lower rate of relapse than patients who receive medication alone.

**BD & Long-term Treatment**

* Long-term Treatment in Bipolar Disorder.*

**Authors:** Swann AC. - From the Department of Psychiatry, University of Texas Medical School, Houston

**Source:** J Clin Psychiatry. 2005 Jan;66 Suppl 1:7-12. Related Articles, Links

**Summary:** Bipolar disorder is a lifelong illness with a course that is usually chronic or recurrent. Severity of complications is generally proportionate to the number of episodes, especially depression. In addition to potentially preventing episodes, effective treatment reduces mortality. This article reviews long-term treatment strategies for bipolar disorder, focusing on depressive episodes, and discusses treatment studies, including problems in design. Treatment effectiveness, including reduction of suicide risk, is enhanced if patients and physicians collaboratively recognize and treat prodromal symptoms, preventing the emergence of episodes. Strategies for treatment differ as one progresses from obtaining syndromal recovery in the acute episode, to functional recovery during continuation treatment, to stability during maintenance treatment. Successful long-term treatment of bipolar disorder requires integrated pharmacologic and nonpharmacologic treatments combined with a therapeutic alliance that facilitates a proactive, preventive approach to the illness.

**BD II, Diagnosis & Management**

* Diagnosis and Management of Patients With Bipolar II Disorder.*

**Authors:** Yatham LN. - From the Division of Mood Disorders, University of British Columbia, Vancouver, Canada


**Summary:** Bipolar II disorder is frequently misdiagnosed as major depressive disorder. In particular, correct diagnosis of bipolar II disorder may be delayed by years due to the predominance of depressive symptoms and the relative subtlety of hypomania, which may manifest only briefly and without elevated mood. The prevalence of bipolar II disorder varies from 0.5% to about 5% depending on the criteria used. Diagnosis can be improved by using mood disorder questionnaires, systematic probing, and prospective mood diary charting. There is a dearth of research into treatment of bipolar disorder. The limited available evidence suggests that lithium and lamotrigine may have efficacy in preventing relapse of mood episodes. Acute bipolar II depression could be treated with a combination of a mood stabilizer plus an antidepressant or pramipexole and in rare cases with antidepressant monotherapy. Hypomania will likely respond to monotherapy with an antimanic agents. Adjunctive psychosocial treatments may provide additional benefit in patients with bipolar II disorder.

**BD, ADHD & Children**

* Recognizing and Managing Bipolar Disorder in Children.*

**Authors:** Wozniak J. - From the Pediatric Psychopharmacology Unit, Massachusetts General Hospital, Boston


**Summary:** Bipolar disorder affects people of all ages, including preschool-aged children. Two major difficulties in diagnosing children with bipolar disorder are its overlap with attention-deficit/hyperactivity disorder (ADHD) and its developmentally distinct presentation from that in adults, with high rates of irritability, chronicity, and mixed states. Comorbid conditions are common in bipolar disorder and, in addition to ADHD, include depression, anxiety disorders, oppositional defiant disorder, and conduct disorder. Family studies have helped to confirm the validity of bipolar disorder in children. In terms of treatment, children do not appear to respond well to conventional mood stabilizers alone. However, using an atypical antipsychotic either alone or in addition to another mood stabilizer has shown utility in treating manic symptoms, depression in mixed states, and aggression. Amphetamine salts have been helpful in treating bipolar children with comorbid ADHD, but no data are available on treating comorbid depression in bipolar children. Because childhood-onset mania is commonly chronic rather than episodic, highly comorbid, and characterized by high rates of irritability, future clinical trials should examine the overlap of mania with other disorders in children to determine routes to accurate diagnosis and treatment.

**MDD, Mirtazapine & Fluoxetine**

* Comparison of the Effects of Mirtazapine and Fluoxetine in Severely Depressed Patients.*

**Authors:** Versiani M, Moreno R, Ramakers-van Moorsel CJ, Schutte AJ. Antidepressants Study Group CE, - Institute of Psychiatry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil.

**Source:** CNS Drugs. 2005;19(2):137-46. Related Articles, Links

**Summary:** INTRODUCTION: Depression is a major global problem associated with large medical, sociological and economic burdens. Mirtazapine (Remeron(R)), Organon NV, The Netherlands) is an antidepressant with a unique mechanism of action that has similar or superior efficacy to TCAs and SSRIs in moderate-to-severe depression. However, this agent has not yet been tested in patients with severe depression alone.OBJECTIVE: To compare the antidepressant efficacy and tolerability of mirtazapine and fluoxetine and their effects on anxiety and quality of life in patients with severe depression (>or=25 points on the first 17 items of the Hamilton Depression Rating Scale [HDRS-17]).METHODS: In this double-blind study, 297 severely depressed patients were randomised to receive mirtazapine 15-60 mg/day (n = 147) or fluoxetine 20-40 mg/day (n = 152) for 8 weeks. 294 subjects were actually treated and 292 included in the intent-to-treat population. Symptom severity was measured by the HDRS-17, Montgomery-Asberg Depression Rating Scale (MADRS) and Clinical Global Impression (CGI) rating scale. Quality of life was self-assessed by patients using the Leeds Sleep Evaluation Questionnaire and the Quality of Life, Enjoyment and Satisfaction Questionnaire. Adverse events were recorded throughout the study.RESULTS: No statistically significant differences were noted between the
two groups in change from baseline HDRS-17 score at any time point; both treatments were associated with large (~15 points) decreases by study end. However, more mirtazapine-treated patients tended to exhibit a >/=/50% decrease in HDRS score (significant at day 7; 9.0% vs 0.7%, p = 0.002). Significant differences in favour of mirtazapine were also observed at day 14 for changes in MADRS scores (~10.9 vs -8.5, p = 0.006) and the proportion of patients with >/=/50% decrease in MADRS score (21.4% vs 10.9%, p = 0.031). On the CGI, the proportion of 'much/very much improved' patients tended to be greater with mirtazapine (significant at day 7; 9.7% vs 3.4%, p = 0.032). No significant between-group differences were observed for the majority of quality-of-life measures. However, mirtazapine produced significantly better improvements on ‘sleeping assessment 1’ (14.9 +/- 5.2 vs 13.7 +/- 5.4, p = 0.028) and ‘sleeping assessment 2’ (p = 0.013) than fluoxetine. Both agents were generally well tolerated but mirtazapine-treated patients experienced a mean weight gain of 0.8 +/- 2.7kg compared with a mean decrease in weight of 0.4 +/- 2.1kg for fluoxetine-treated patients (p < 0.001). Conclusions: Mirtazapine is as effective and well tolerated as fluoxetine in the treatment of patients with severe depression.

CVRFs & Depressive symptoms —

Risk factors for geriatric depression: the importance of executive functioning within the vascular depression hypothesis.

Authors: Mast BT, Yochim B, Macneill SE, Lichtenberg PA. - Psychological and Brain Sciences, 317 Life Sciences, University of Louisville, Louisville, KY 40292, b.mast@louisville.edu.


Summary: BACKGROUND: Results from recent studies addressing the vascular depression hypothesis have been mixed, with cerebrovascular risk factors (CVRFs) predicting depression in some geriatric patients but not in others. The current study seeks to examine executive dysfunction as a potential moderator of the relationship between CVRFs and depressive symptoms. METHODS: Data concerning CVRFs, executive functioning, and depressive symptoms from 77 geriatric rehabilitation patients were incorporated to test the hypothesis that patients with executive dysfunction and greater CVRFs would demonstrate the highest levels of depression over time. CVRFs (diabetes, hypertension, atrial fibrillation) were measured via diagnosis by treating physician. Depression was assessed using the 15-item Geriatric Depression Scale (GDS) at baseline and at 6-month and 18-month follow-ups. Executive functioning was measured at baseline using the Initiation/Perseveration (IP) Subtest of the Mattis Dementia Rating Scale. RESULTS: Multivariate analysis of variance demonstrated a significant statistical interaction between the number of CVRFs and scores on the IP Subtest on depressive symptoms. Patients with two or more CVRFs and lower IP scores demonstrated significantly greater depressive symptoms at baseline and at 18-month follow-up than patients with fewer CVRFs and higher IP scores. The univariate effect at 6 months was not significant. Conclusion: The current data suggest that scores on an index of executive functioning may moderate the relationship between CVRFs and depressive symptoms. Interpretation of these findings is provided in the context of the vascular depression hypothesis and related frontotemporal dysfunction. Patients with greater CVRF burden and poor executive functioning may be at particularly high risk for depression.

BD & Mood changes —

Mood changes related to antidepressants: a longitudinal study of patients with bipolar disorder in a naturalistic setting.

Authors: Bauer M, Rasgon N, Grof P, Alshuler L, Gyalui L, Lapp M, Glenn T, Whybrow PG. - Department of Psychiatry and Psychotherapy, Charite-University Medicine Berlin, Campus Charite-Mitte (CCM), Schumannstr. 20/21, 10117 Berlin, Germany; Neuropsychiatric Institute & Hospital, Department of Psychiatry and Biobehavioral Sciences, University of California Los Angeles (UCLA), 760 Westwood Plaza, Los Angeles, CA, 90024, USA.

Source: Psychiatry Res. 2005 Jan 30;133(1):73-80. Related Articles, Links

Summary: This prospective, longitudinal study investigated the frequency and pattern of mood changes between outpatients receiving usual care for bipolar disorder who were either taking or not taking antidepressants. Eighty patients with bipolar disorder self-reported mood and psychiatric medications daily for 3 months using a computerized system (ChronoRecord) and returned 8662 days of data. Of the total group of 80 patients, 47 took antidepressants; 33 did not. Patients taking antidepressants reported depression twice as frequently (29% of days vs. 13.8% of days). In both groups, two-thirds of all mood changes over a 1-, 2- and 3-day period were small, between -5 and 5 on a 100-point scale. No statistically significant difference was found in the frequency of large mood changes (>10 on a 100-point scale) or in switches between depression and mania (0.7% if not taking antidepressants vs. 0.9% if taking), independent of diagnosis of bipolar I or II. Eighty-nine percent of patients taking antidepressants were also taking mood stabilizers. In this naturalistic setting, no significant difference between the rate of switches to mania or rapid cycling was found between those taking and not taking antidepressants, regardless of diagnosis. The primary difference in pattern between the groups was the time spent in depressed or normal mood, with minor daily mood variations.

BD II & Mixed depression —

Mixed depression: a clinical marker of bipolar-II disorder.

Authors: Benazzi F. - E. Hecker Outpatient Psychiatry Center, Ravenna, Italy; University of California at San Diego Collaborating Center, USA; Department of Psychiatry, National Health Service, Forli, Italy.


Summary: BACKGROUND: Recent studies have found that mixed depression [i.e., a major depressive episode (MDE) plus intra-MDE hypomanic symptoms] is common in bipolar-II disorder (BP-II), and not uncommon in major depressive disorder (MDD) depressed outpatients. Study aim was to test the predictive power for the diagnosis of BP-II of several dimensional definitions of mixed depression, searching for a clinical marker which could reduce the current underdiagnosis of BP-II. METHODS: Consecutive 348 BP-II and 254 MDD depressed outpatients were interviewed by the Structured Clinical Interview for DSM-IV, the Hypomania Interview Guide, and the Family History Screen, by a senior psychiatrist in a private practice. Intra-MDE hypomanic symptoms were systematically assessed. Mixed depression was defined as an
MDE plus intra-MDE hypomanic symptoms. RESULTS: Dimensional definitions of mixed depression (at least 2, 3, 4, 5 or more intra-MDE hypomanic symptoms) were tested for predicting BP-II. A definition requiring 2 or more hypomanic symptoms had the highest sensitivity, the lowest specificity, and the lowest positive predictive value. A definition requiring 5 or more hypomanic symptoms had the highest specificity, the lowest sensitivity, and the highest positive predictive value. The most balanced combination of sensitivity and specificity was found for a definition requiring 3 or more hypomanic symptoms. This definition had the highest positive predictive value, and the highest ROC area (i.e., the best global performance). This definition also had the most balanced combination of sensitivity and specificity for predicting bipolar family history. In order to validate this definition as a clinical marker of BP-II, as bipolar validators were used BP-II, young onset, many recurrences, atypical depression features, and bipolar family history (the most important one). Univariate logistic regression found that this definition was associated with most bipolar validators, especially bipolar family history. Multiple logistic regression found that bipolar family history was its strongest predictor. Conclusions: Findings suggest that a definition of mixed depression requiring 3 or more intra-MDE hypomanic symptoms may be a useful clinical marker for predicting the diagnosis of BP-II. Presence of mixed depression should lead to skillful probing for history of hypomania, which would probably reduce the BP-II misdiagnosed as MDD. Findings may also impact treatment of BP-II, as intra-MDE hypomanic symptoms may become more severe by antidepressants alone, and mood stabilising agents may be required before (or concurrently with) antidepressants.

**GSP, Glutamatergic & GABAergic anticonvulsant — An Open Trial of Topiramate in the Treatment of Generalized Social Phobia.**

**Authors:** Van Ameringen M, Mancini C, Pipe B, Oakman J, Bennett M. - From the Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton (Drs. Van Ameringen and Mancini); the Anxiety Disorders Clinic, McMaster University Medical Centre of Hamilton Health Sciences, Hamilton (Drs. Van Ameringen and Mancini, Ms. Pipe, and Mr. Bennett); and the Department of Psychology, University of Waterloo, Waterloo (Dr. Oakman), Ontario, Canada

**Source:** J Clin Psychiatry. 2004 Dec;65(12):1674-1678. Related Articles, Links

**Summary:** BACKGROUND: Selective serotonin reuptake inhibitors (SSRIs) are the current gold standard in the pharmacologic treatment of generalized social phobia. SSRIs are only effective in approximately 50% of individuals with generalized social phobia and can be associated with significant side effects. Based on the successful use of the anticonvulsants gabapentin and pregabalin in treating generalized social phobia, we conducted an open trial examining the efficacy of the glutamatergic and GABAergic anticonvulsant topiramate in the treatment of generalized social phobia. METHOD: Twenty-three adult outpatients with DSM-IV social phobia, generalized type, were entered into a 16-week open trial of topiramate, starting at 25 mg/day, and gradually titrated up to a maximum dose of 400 mg/day. RESULTS: Twelve of 23 patients completed the trial. In the intent-to-treat (ITT) analysis, 11 (47.8%) of 23 were responders by a Clinical Global Impressions Improvement (CGI-I) scale rating of "much" or "very much" improved. The mean drop in the Liebowitz Social Anxiety Scale (LSAS) score for the ITT group was 29.4%. The change in LSAS score from baseline to endpoint was significant for the ITT group (F = 3.44, df = 4,110; p = .01). In the completers group, 9 (75.0%) of 12 were responders by CGI-I at 16 weeks, with a mean drop in LSAS score of 45.1%. The rate of remission in the ITT sample, using a definition of an LSAS score of < 30, gave a remission rate of 26.1% (6/23). Conclusion: This study suggests that topiramate may be effective in the treatment of generalized social phobia. These results also suggest the possibility that the neurotransmitters glutamate and GABA may be involved in the neurobiology of generalized social phobia.

**SP, Neurobiology & Pharmacotherapy — [Neurobiology and Pharmacotherapy of Social Phobia]**

**Authors:** Aouizerate B, Martin-Guehl C, Tignol J. Service de Psychiatrie d’Adultes, (Professeur Tignol) - Universite Victor-Segalen Bordeaux 2, Centre Hospitalier Charles-Perrens, Bordeaux, France

**Source:** J Clin Psychiatry. 2004 Apr;65(4):546-554. Links, Related Articles

**Summary:** BACKGROUND: The neurobiological aspects of social anxiety disorder (SAD) are only beginning to be explored. Depression, anxiety, and SAD may all be related to alterations in neural systems. Currently, most research on SAD has focused on serotonin (5-HT) and excitatory amino acid (EAA) neurotransmitters. Recent evidence has suggested that a dysfunction in glutamatergic neurotransmission may be involved in the pathogenesis of SAD. Recent work in our laboratory has demonstrated that glutamatergic neurotransmission is altered in SAD. This study was conducted to determine the extent to which topiramate, a new anticonvulsant that has been reported to have both GABAergic and glutamatergic effects, improves social anxiety disorders.

**Conclusions:** Topiramate was found to be efficacious in treating generalized social phobia. The results of this study suggest that topiramate may be a useful treatment for social anxiety disorders. Future studies should investigate the mechanisms by which topiramate acts to improve social anxiety disorders.
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Summary: Social phobia (also known as social anxiety disorder) is still not clearly understood. It was not established as an authentic psychiatric entity until the diagnostic nomenclature of the American Psychiatric Association DSM III in 1980. In recent years, increasing attention among researchers has contributed to providing important information about the genetic, environmental, and temperamental bases of social phobia and its neurochemical, neuroendocrinological and neuroanatomical substrates, which remain to be further investigated. Up to date, there have been several findings about the possible influence of variables, including particular genetic, socio-familial and early temperamental (e.g., behavioral inhibition) factors that represent risk for the later development of social phobia. Clinical neurobiological studies, based on the use of exogenous compounds such as lactate, CO2, caffeine, epinephrine, flumazenil or cholecystokinin/pentagastrin to reproduce naturally occurring phobic anxiety, have shown that patients with social phobia appear to exhibit an intermediate sensitivity between patients with panic disorder and control subjects. No difference in the rate of panic attacks in response to lactate, low concentrations of CO2 (5%), epinephrine or flumazenil was observed between patients with social phobia and normal healthy subjects, both being less reactive compared to patients with panic disorder. However, patients with social phobia had similar anxiety reactions to high concentrations of CO2 (35%), caffeine or cholecystokinin/pentagastrin than those seen in patients with panic disorder, both being more intensive than in controls. Several lines of evidence suggest specific neurotransmitter system alterations in social phobia, especially with regard to the serotonergic, noradrenergic and dopaminergic systems. Although no abnormality in platelet serotonin transporter density has been found, patients with social phobia appear to show an enhanced sensitivity of both pre- and post-synaptic 5HT1A and 5HT2 serotonin receptor subtypes, as reflected by increased anxiety and hormonal responses to serotonergic probes. Platelet 5HT2 receptor density has also been reported to be positively correlated to symptom severity in patients with social phobia. During anticipation of public speaking, heart rate was elevated in patients with social phobia compared to controls. Norepinephrine response to the orthostatic challenge test or to the Valsalva maneuver was also greater in patients with social phobia. While normal beta-adrenergic receptor number was observed in lymphocytes, a blunted response of growth hormone to clonidine, an a2-adrenergic agonist, was reported. This suggests reduced post-synaptic a2-adrenergic receptor functioning related to norepinephrine overactivity in social phobia. Decreased cerebrospinal fluid levels of the dopamine metabolite homovanillic acid have also been observed. There are relatively few reports of involvement of the adrenomedullary and thyroid functions in social phobia, and all that has been noted is that patients with social phobia show an exaggerated adrenocortical response to a psychological stressor. Recent advances in neuro-imaging have contributed to find low striatal dopamine D2 receptor binding or low dopamine transporter site density in patients with social phobia. They have also demonstrated the involvement of the cortico-limbic pathways, including the prefrontal cortex, hippocampus and amygdala, which show an increased activity in different experimental conditions. These brain regions have extensively been reported to play an important role in the cognitive appraisal in determining the significance of environmental stimuli, in the emotional and mnemonic integration of information, and in the expression of contextual fear-conditioned behaviors, which might be disrupted in the light of the phenomenological aspects of social phobia. A substantial body of literature based on case reports, open and placebo-controlled trials, has now clearly examined the efficacy of major classes of psychotrophic agents including monoamine oxidase inhibitors, beta-blockers, selective serotonin reuptake inhibitors and benzodiazepines in social phobia. Until recently, irreversible non-selective monoamine oxidase inhibitors, of which phenelzine was the most extensively evaluated, were considered as the most efficacious treatment in reducing the symptomatology associated with social phobia in 50-70% of cases after 4 to 6 weeks. However, side effects and dietary restrictions limit their use. This led to the development of reversible inhibitors of monoamine oxidase A, for which careful dietary monitoring is not required. Moclobemide has been the most widely studied but produced unconvincedly therapeutic effects on social phobic symptoms. To date, selective serotonin reuptake inhibitors may be considered as a reasonable first-line pharmacotherapy for social phobia. There is growing evidence for the efficacy of the selective serotonin reuptake inhibitors fluvoxamine, fluoxetine, citalopram, paroxetine and sertraline. They have beneficial effects with response rates ranging from 50 to 80% in social phobia. It has been recommended that the treatment period should be extended at least 6 months beyond the early improvement achieved within the first 4 to 6 weeks. The overall advantages include tolerability with a low risk of adverse events. The benzodiazepines clonazepam and alprazolam have also been proposed for the treatment of social phobia. Symptomatic relief occurred in 40 to 80% of the cases with a relatively rapid onset of action within the first two weeks. Untoward effects, discontinuation-related withdrawal symptoms and abuse or dependence liability constitute major concerns about the use of benzodiazepines, so they should be reserved for cases unresponsive to the safer medications cited above. Beta-blockers such as atenolol and propranolol have commonly been employed in performance anxiety, decreasing autonomic symptoms (e.g., tachycardia, sweating and dry mouth). However, they are not effective in the generalized form of social phobia. Other pharmacologic alternatives seem helpful for the management of social phobia, including venlafaxine, gabapentin, bupropion, nefazodone or augmentation with bupropine. Preliminary studies point to promising effects of these agents. Larger controlled clinical trials are now needed to confirm their potential role in the treatment of social phobia.

Nicotine treatment & OCD

Author: Lundberg S, Carlsson A, Norfeldt P, Carlsson ML. Psychiatric Clinic, Kungalvs Sjukhus, Kungalv, Sweden


Summary: Following initial observations of marked effects of nicotine self-medication in a patient with obsessive-compulsive disorder (OCD), another four OCD patients were treated with nicotine for eight weeks in an open label fashion. Patients fulfilling DSM-IV criteria for OCD and with initial Yale-Brown Obsessive-Compulsive Scale (YBOCS) score>15 were included in the study. The patients were scored with YBOCS, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), NIMH Global Obsessive-Compulsive Scale (NIMH) and Global

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Assessment of Functioning (GAF). Four of five patients receiving nicotine treatment displayed a favourable response with reductions in YBOCS scores. For these four patients, the nicotine chewing gum enabled a more adequate behaviour in stressful, OCD-eliciting, situations. We feel that these results are encouraging enough to warrant a larger, controlled study on nicotine treatment of OCD.

**OCD & Nicotine**


**Authors**: Pasqui M, Garavini A, Biondi M. - Psychiatric Clinic III, University of Rome La Sapienza, Viale dell’Università, 30; 00185 Roma, Italy. maxparasqua@tiscali.net.it


**Summary**: The authors present a case of obsessive-compulsive disorder (OCD) resistant to conventional treatments, which improved following nicotine augmentation administered as 4 mg chewing gum. The role of acetylcholine in the pathophysiology of OCD is not clear. The authors discuss the effect of nicotine on memory for actions.

**EDS & PD**

- Sleep episodes and daytime somnolence as result of individual susceptibility to different dopaminergic drugs in a PD patient: a polysomnographic study.

**Authors**: Romigi A, Brusa L, Marciani MG, Pierantozzi M, Piacidi F, Izza F, Sperli F, Testa F, Stanzone P. - University of Rome "Tor Vergata" Policlinico Tor Vergata Servizio di Neurofisiopatologia, Centro di Medicina del Sunno, Italy; IRCCS Fondazione Santa Lucia Via Ardeatina 306 Rome, Italy


**Summary**: The association between excessive daytime somnolence (EDS) and idiopathic Parkinson’s disease (PD) is often reported but still debated. The possible role of antiparkinsonian therapy or primarily of PD on excessive diurnal sleepiness is controversial. We describe the case of a 61-year-old patient affected by PD who experienced sleep episodes (SE) occurring during pramipexole plus l-Dopa therapy. Polysomnographic sleep studies and subjective evaluations of daytime sleepiness (Epworth Sleepiness Scale) were carried out under administration of pramipexole plus l-Dopa, l-Dopa monotherapy and cabergoline plus l-Dopa. The polysomnography revealed two sleep events during pramipexole plus l-Dopa. Moreover, the polysomnographic data showed an increase of both diurnal and nocturnal sleep under pramipexole plus l-Dopa compared with cabergoline plus l-Dopa and l-Dopa as monotherapy. In addition, while Epworth Sleepiness Scale (ESS) Score showed a mild sleepiness under pramipexole (ESS score=11), ESS scores were normal under both l-Dopa and cabergoline plus l-Dopa. Sleep episodes also disappeared under both l-Dopa and cabergoline plus l-Dopa (2- and 12-month follow-up). We hypothesize that an individual susceptibility to specific antiparkinsonian drug may play a significant role in the genesis of sleepiness in our PD patient.

**APD & Social avoidance**

- Is avoidant personality disorder more than just social avoidance?

**Authors**: Taylor CT, Laposa JM, Alden LE. - University of British Columbia, Vancouver, Canada

**Source**: J Personal Disord. 2004 Dec;18(6):571-94. Related Articles, Links

**Summary**: Although social avoidance is a defining feature of avoidant personality disorder (APD), some theorists posit that APD is characterized by a broader pattern of avoidance that extends beyond social situations. This paper describes a series of four studies that examined the different types of nonsocial avoidance hypothesized to characterize APD in three undergraduate student samples and a clinical sample of adults with APD. Overall, the findings revealed low to moderate associations between APD and emotional and novelty avoidance, as well as avoidance of various nonsocial events. The results provide support for contemporary models of APD.

**PDs, Adolescent & Conflict**

- Adolescent personality disorders and conflict with romantic partners during the transition to adulthood.

**Authors**: Chen H, Cohen P, Johnson JG, Kasen S, Sneed JR, Crawford TN. - Department of Epidemiology, New York State Psychiatric Institute, USA. hc657@columbia.edu


**Summary**: Longitudinal data were used to investigate the association of adolescent personality disorders with conflict between romantic partners during the transition to adulthood (i.e., age 17 to 27). Findings indicated that adolescent personality disorders (PDs) assessed at mean age 16 were associated with subsequent elevated partner conflict. Cluster B PD was associated with sustained elevations in partner conflict throughout the transition to adulthood. Cluster A and C PDs were associated with elevated partner conflict before age 23. Paranoid, schizoid, schizotypal, borderline, narcissistic, and obsessive-compulsive PD symptoms were independently associated with sustained elevations in partner conflict.

**PD, Adolescent & Stability**

- Two-year stability of personality disorder in older adolescent outpatients.

**Authors**: Chanen AM, Jackson HJ, McCoy GR, Allot KA, Clarkson V, Yuen HP. - ORYGEN Research Centre, Department of Psychiatry, University of Melbourne. achanen@unimelb.edu.au

**Source**: J Personal Disord. 2004 Dec;18(6):526-41. Related Articles, Links

**Summary**: The 2-year stability of categorical and dimensional personality disorder (PD) in an older adolescent psychiatric outpatient sample was examined. One hundred and one 15-18-year-old participants were assessed using the Structured Clinical Interview for DSM Axis II Disorders (SCID-II) at baseline and 97 were re-interviewed, face-to-face, at 2 years. Of those with a categorical PD diagnosis at baseline, 74% still met criteria for a PD at follow-up, with marked gender differences (83% of females and 56% of males). Kappa for specific PDs was low for all except antisocial. Rank order and mean level dimensional stability ranged from high (antisocial, schizoid) to moderate.
Articles, Links especially for some cluster A and B PDs. Diagnosis and early intervention appears to be justified in this age group.

Trichotillomania

- [Trichotillomania, Its Course and Psychosocial Consequences] [Article in Polish]
Summary: The article contains the definition and characteristics of trichotillomania, its prevalence, main syndromes and factors which intensify the pressure of uncontrolled hair pulling. It also raises the problem of the role of tension in maintaining these behaviours what is connected with some controversy around the definition of trichotillomania. In addition this article includes its relationship with other mental disorders. Special attention was given to the subjective experiences of chronic hair-pulling, and to social and psychological consequences of trichotillomania.

Traumatic experience & Coping style

- [Coping with stress in those who experienced a traumatic situation] [Article in Polish]
Summary: AIM: Does the traumatic experience influence the choice of a particular coping style? If yes, which style is preferred by those who experienced trauma? Answering these two essential questions is the aim of this paper. The authors have accepted the assumption (Holman, Silver, 1998), that the individuals who experienced trauma prefer past temporal orientation and they present a higher level of distress. METHOD: The authors investigated two groups. The experimental group consisted of 46 victims of the Gdańsk Shipyard concert hall fire. The control group comprised the 41 individuals who never experienced any trauma. Two psychological methods were used. CISS--Endler and Parker, which measures coping styles. STAI--Spielberger and al., was the second method used for measuring the level of anxiety as an essential distress indicator. RESULTS AND Conclusions: The results show, that individuals who experienced trauma, presented a significantly higher level of anxiety and that the victims of trauma prefer the emotional coping style. The difference is statistically significant. There is also an indirect conclusion (based on these results), which confirms the above mentioned assumption.

5-HT & 5-HTT in PD

- Reduced brain serotonin transporter binding in patients with panic disorder.
Summary: There is strong evidence for the importance of the serotonin (5-HT) system in the neurobiology of panic disorder (PD); however, the exact role of this system remains unclear. The 5-HT transporter (5-HTT) is a key element in 5-HT neurotransmission. The current study aimed to investigate the binding of 5-HTT in the brain of patients with PD. We used single-photon emission computed tomography with a radioligand that specifically labels the 5-HTT, [(123)I]nor-beta-CIT. Subjects comprised eight patients with current PD, eight patients with PD in remission, and eight healthy control subjects. The patients with current PD showed a significant decrease in 5-HTT binding in the midbrain, in the temporal lobes and in the thalamus in comparison to the controls. The binding of 5-HTT in patients with PD in remission was similar to findings in the control group in the midbrain and in the temporal lobes, but lower in the thalamus. Regional 5-HTT binding significantly and negatively correlated with the severity of panic symptoms. These findings point to a dysregulation of the 5-HT system in PD patients. Altered function of 5-HTT appears to be related to the clinical status of patients. Clinical improvement in the patients in remission is associated with normalization of 5-HTT binding.

PD, Agoraphobia & Depression

- A Prospective Evaluation of Agoraphobia and Depression Symptoms Following Panic Attacks in a Community Sample of Adolescents.
Authors: Wilson KA, Hayward C. - Department of Psychiatry and Behavioral Sciences, Stanford University Medical Center, 401 Quarry Road, Stanford, CA 94305-5722, USA. kawilson@stanford.edu Source: J Anxiety Disord. 2005;19(1):87-103. Related Articles, Links
Summary: In a community sample of high schoolers who experienced their first panic attack, we examined the prospective relationships among pre-panic vulnerabilities, panic attack severity, and post-panic agoraphobia and depression symptoms. Students were evaluated yearly over 4 years to test the following four hypotheses: (1) pre-panic anxiety sensitivity, negative affect, and childhood behavioral inhibition will serve as vulnerabilities that predict agoraphobia and depression symptoms following a panic attack; (2) these vulnerabilities will lead to more severe panic attacks; (3) severe and spontaneous panic attacks will predict subsequent agoraphobia and depressive symptoms; and (4) the interaction between panic severity and vulnerabilities will be associated with worse outcomes following a panic attack. Results supported the first three hypotheses, but no evidence emerged for an interactive effect. Findings are discussed in light of recent modernized classical conditioning models that address factors contributing to development of more severe panic related psychopathology after panic attacks.

OCD & ACC

- Error-related hyperactivity of the anterior cingulate cortex in obsessive-compulsive disorder.
Authors: Fitzgerald KD, Welsh RC, Gehring WJ, Abelson JL, Students were evaluated yearly over 4 years to test the following four hypotheses: (1) pre-panic anxiety sensitivity, negative affect, and childhood behavioral inhibition will serve as vulnerabilities that predict agoraphobia and depression symptoms following a panic attack; (2) these vulnerabilities will lead to more severe panic attacks; (3) severe and spontaneous panic attacks will predict subsequent agoraphobia and depressive symptoms; and (4) the interaction between panic severity and vulnerabilities will be associated with worse outcomes following a panic attack. Results supported the first three hypotheses, but no evidence emerged for an interactive effect. Findings are discussed in light of recent modernized classical conditioning models that address factors contributing to development of more severe panic related psychopathology after panic attacks.

Paroxetine treatment was significantly superior to placebo at weeks 3 through 12 on the Liebowitz Social Anxiety Scale, the Clinical Global Impression-Severity of Illness scale, and the Social Phobia Inventory, and at weeks 4 through 12 for response (P < .05 for all). Week 12 response rates were significantly greater for the venlafaxine ER and paroxetine groups (58.6% and 62.5%, respectively) vs the placebo group (36.1%) (P < .001 for both). Conclusion: Venlafaxine ER is effective in the short-term treatment of generalized social anxiety disorder, with efficacy and tolerability comparable to paroxetine.

**Child & Adolescent psychiatry**

**Atypical – antipsychotics in children and Adolescents**

* Second-generation antipsychotic medications in children and adolescents.

**Authors**: Cheng-Shannon J, McGough JJ, Pataki C, McCracken JT. - Department of Psychiatry, University of Washington School of Medicine, Seattle, WA, USA

**Source**: J Child Adolesc Psychopharmacol. 2004 Fall;14(3):372-94. Related Articles, Links

**Summary**: OBJECTIVE: We reviewed available pediatric literature on second-generation antipsychotic medications to assess current evidence of efficacy and safety. METHOD: An English language MEDLINE search (1974-2003) was conducted using key words-atypical antipsychotics, children and adolescents, toxicity, clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole. Additional efficacy and safety data were obtained from drug manufacturers. RESULTS: We identified 176 reports, including 15 double-blind, controlled trials, 58 open-label studies, 18 retrospective chart reviews, and 85 case series/reports. The majority of these studies (43%) were of risperidone. Evidence suggests that second-generation antipsychotics are efficacious in the treatment of psychosis, bipolar disorders, pervasive developmental disorders, and Tourette’s Disorder, and are potentially useful in mental retardation, conduct disorder, and severe attention deficit hyperactivity disorder (ADHD). The most frequently reported side effects included cardiovascular effects, weight gain, sedation, sialorrhea, extrapyramidal signs, and hyperprolactinemia, although the relative frequencies of these untoward effects vary among medications. **Conclusion:** Although the evidence base for pediatric use of second-generation antipsychotics is expanding, the majority of available studies are anecdotal, or short-term, open-label trials. Reports suggest that these compounds are effective for a variety of psychiatric disorders in children and adolescents, but additional double-blind, controlled studies are required to establish definitive efficacy. Although these medications appear to be well tolerated in short-term studies, long-term follow-up investigations and ongoing clinical monitoring are necessary to confirm their safety in this age group.

**Adolescents & Suicide**

* Treatment for adolescents following a suicide attempt: results of a pilot trial.

**Authors**: Donaldson D, Spirito A, Esposito-Smythers C. Dr. Donaldson is with the May Institute, Norwood, MA, and Brown Medical School, Providence, RI; Drs. Spirito and Esposito-Smythers are with Brown Medical School, Providence, RI.

**Summary**: OBJECTIVE: The purpose of this study was to determine the clinical features of adolescents who have attempted suicide and to identify risk factors associated with a history of suicide attempts. METHOD: A retrospective chart review was conducted on 47 adolescents who attempted suicide. RESULTS: Adolescents who had a history of suicide attempts were more likely to have a family history of suicide and to be experiencing a precipitating event. Adolescents who had made multiple attempts were more likely to have a family history of suicide, to be depressive, and to have a history of substance abuse. Conclusion: Adolescents who have attempted suicide are at increased risk for future attempts and may require additional intervention. **Conclusion:** Adolescents who have attempted suicide are at increased risk for future attempts and may require additional intervention.

**GSAD, Venlafaxine ER & Paroxetine**

* Venlafaxine extended release vs placebo and paroxetine in social anxiety disorder.

**Authors**: Liebowitz MR, Gelenberg AJ, Munjack D. - New York State Psychiatric Institute, New York 10032, USA.

**Source**: Arch Gen Psychiatry. 2005 Feb;62(2):190-8. Related Articles, Links

**Summary**: BACKGROUND: Evidence indicates that venlafaxine hydrochloride extended release (ER) effectively ameliorates anxiety symptoms. OBJECTIVES: To evaluate the efficacy, safety, and tolerability of flexible-dose venlafaxine ER compared with placebo in the short-term treatment of generalized social anxiety disorder and, secondarily, to compare paroxetine with venlafaxine ER and paroxetine with placebo. DESIGN: Adult outpatients with DSM-IV generalized social anxiety disorder for 6 months or longer were randomly assigned to receive venlafaxine hydrochloride ER (75-225 mg/d), paroxetine (20-50 mg/d), or placebo for 12 weeks or less at 26 centers in the United States. The primary outcome measure was the total Liebowitz Social Anxiety Scale score. Secondary measures included response (Clinical Global Impression-Improvement score, 1 or 2) and Clinical Global Impression-Severity of Illness and Social Phobia Inventory scores. RESULTS: Of 440 patients treated, 413 (93.9%) were included in the last-observation-carried-forward efficacy analysis; of the 429 patients in the safety population, 318 (74.1%) completed the study. Mean daily doses were 201.7 mg (SD, 38.1 mg) of venlafaxine hydrochloride ER and 46.0 mg (SD, 7.9 mg) of paroxetine. Venlafaxine ER treatment was significantly superior to placebo at weeks 1 through 12 on the Liebowitz Social Anxiety Scale and Social Phobia Inventory and at week 2 and weeks 6 through 12 for Clinical Global Impression-Severity of Illness and responder status, and was significantly superior to paroxetine treatment at weeks 1 and 2 for the Social Phobia Inventory (P < .05 for all).
Autism & Chromosome 15 ——

*Autistic spectrum disorder associated with partial duplication of chromosome 15; three case reports.*

**Authors:** Simic M, Turk J. - Michael Rutter Centre for Children and Young People, The Maudsley Hospital, London SE5 8AZ, UK. mima.simic@slam.nhs.uk

**Source:** Eur Child Adolesc Psychiatry. 2004 Dec;13(6):389-93. Related Articles, Links

**Summary:** Duplication of part or the entirety of chromosome 15 that involves the Prader-Willi/Angelman syndrome critical region (PWACR) is a genetic disorder which is associated with variable degrees of intellectual impairment, motor co-ordination problems and social and communication disorders. Published case reports indicate that phenotypic expression is dependent on parental origin of the duplication and implicate maternally derived duplications in the pathogenesis of autistic features. This article describes three individuals, two males and one female, aged between 5 and 8 years, all with partial duplication of chromosome 15. Autism (or autistic spectrum disorder) was present in all three instances with varying degrees of cognitive impairment. The aim of this paper is to describe the phenotypic characteristics of this genetic sequence and the possible associations between social and behavioural patterns on the one hand, and degree and nature of genetic impairment on the other.

Autism & Tuberous sclerosis ——

*Autism in tuberous sclerosis.*

**Authors:** Curatolo P, Porfirio MC, Manzi B, Seri S. - Department of Neurosciences, Pediatric Neurology Unit, Tor Vergata University of Rome, Via di Tor Vergata 135, 00133 Rome, Italy. curatolo@uniroma2.it

**Source:** Eur J Paediatr Neurol. 2004;8(6):327-32. Related Articles, Links

**Summary:** Despite considerable progress in the last few years, the neurobiologic basis of autism in tuberous sclerosis complex is still largely unknown and its clinical management represents a major challenge for child neurologists. Recent evidence suggests that early-onset refractory epilepsy and functional deficits associated with the anatomical lesions in the temporal lobes may be associated with autism. No one factor alone (cognitive impairment, tuber localization, occurrence of infantile spasms, focal EEG abnormalities), can be causally linked with the abnormal behaviour. Autism may also reflect a direct effect of the abnormal genetic program. Incidence of autism associated with Tuberous Sclerosis may be significantly higher than the rates of cardiac and renal abnormalities, for which screening is routinely conducted in this population. Hopefully, early diagnosis of autism will allow for earlier treatment and the potential for better outcome for children with Tuberous Sclerosis.

SP & Children  ——

* [Social phobia in children and adolescents] [Article in Polish]

**Authors:** Dabkowska M. - Kliniki Psychiatrii AM w Bydgoszczy


**Summary:** Epidemiological data indicate that anxiety disorders are the most common childhood disorders. 1% of children and adolescents suffer from social phobia and it may influence further adult life. The aim of the article is to show differences of child and adolescent social phobia and its diagnostic criteria. Contrast and distinction of childhood social phobia symptoms are also shown, such as risk factors of appearance of childhood social phobia. The article presents main therapeutic methods—psychotherapy and pharmacotherapy applied to children with phobia and difficulties with estimating efficacy of the particular therapy in this group of patients. Phobic children perceive surroundings more negatively. They have reduced estimations of their own competency to cope with danger. They also show cognitive impairments of ambiguous situations. As much as 60% children with social phobia suffer from a second, concurrent disorder. Widening of information about symptoms and therapeutic methods may reduce the intensity of the disorder during adulthood.

ADHD - A & Retard stimulants  ——

* [The effectiveness of stimulants of retard forms of children and adolescents with ADHD—a systematic overview] [Article in German]

**Authors:** Sevacek K, Dopfner M, Lehmkuhl G. - Klinik und Poliklinik für Psychiatrie und Psychotherapie des Kindes- und Jugendalters am Klinikum der Universität zu Köln.

**Source:** Z Kinder Jugendpsychiatr Psychother. 2004 Nov;32(4):265-78. Related Articles, Links

**Summary:** Stimulants are the matter of choice to treat attention deficit/hyperactivity disorder (ADHD) pharmacologically. The period of effectiveness of immediate release stimulants is, however, often not satisfying. Currently a variety of retarded forms of methylphenidate and also amphetamine were developed in order to minimize the problems involved in a daily dose. This paper presents the clinical studies on effectiveness, period of effectiveness and the profile of side effects of different forms of stimulants. In the clinical practice the new retard products are effective alternatives. There is an advantage in giving this drug in a once daily single dose. At the same time, the side effects that are caused by an extended period of being effective have to be studied in detail. A more exact adaptation to the requirements of daily obligations and needs of children and adolescents is difficult to realize. Future research is supposed to test schemes of titration including immediate and sustained released stimulants.
ADHD, MPH & Hyperkinetic symptoms

* (Does a morning dose of Methylphenidate Retard reduce hyperkinetic symptoms in the afternoon?) [Article in German]

Authors: Sinzig JK, Doepfner M, Puck J, Banaschewski T, Stephani U, Lehmkuhl G, Rothenberger A; Arbeitsgruppe Methylphenidat. - Klinik fur Psychiatrie und Psychotherapie des Kindes- und Jugendalters am Klinikum der Universitat Koln


Summary: OBJECTIVES: In order to treat children with Attention-deficit/Hyperactivity Disorder (ADHD) with a once-a-day stimulant several galenic approaches have been tried. The long acting methylphenidate (MPH, Medikinet-Retard) is a preparation with a two-step dynamic to release MPH (step one: acute; step two: prolonged). The efficacy of Medikinet-Retard, a new long-acting methylphenidate preparation, is analyzed based on the assessment of parents in the afternoon. METHODS: In a multicenter drug treatment study (placebo controlled, randomized, double-blind) 85 children (normal intelligence, age 6 to 16 years, diagnosis of ADHD according to DSM-IV) were investigated over 4 weeks with weekly visits. Forty-three children received Medikinet-Retard and forty-two children placebo. The weekly dose titration depending on body weight and symptomatology allowed a final maximum of 60 mg. The effects on ADHD as perceived by the parents were assessed weekly with a German symptom checklist for ADHD according to DSM-IV and ICD-10 (FBB-HKS). The differences between baseline and last week of treatment were compared statistically between groups. RESULTS: There was a large and statistically significant positive drug effect on ADHD symptomatology. The effect size of these differences was $\delta = 1.2$ (total score). Effects were found on inattention, hyperactivity and impulsivity on the respective subscales. The efficacy of Medikinet-Retard was evaluated by the parents on an average as good. The rate of responders was four-times higher in the verum-group. The correlations of the changed scores in the parent ratings with the respective change scores in the teacher ratings were in the medium range.

Conclusion: This is the first study with a German long-acting methylphenidate preparation (Medikinet-Retard). According to data based on parents' assessments, the drug showed very good clinical efficacy and safety in children with ADHD. Its two step galenic release of methylphenidate seems to be appropriate for a once-a-day (morning) stimulant in schoolchildren.

DA, Alcoholism & Neurobiology

* Dopamine and alcoholism: neurobiological basis of ethanol abuse.

Authors: Tupala E, Tiihonen J. - Department of Forensic Psychiatry, University of Kuopio, Niuvanniemi Hospital, FIN-70240 Kuopio, Finland. erkki.tupala@niuva.fi


Summary: The role of the dopamine (DA) system in brain reward mechanisms and the development of substance abuse has been well established. We review earlier animal and human studies on DA and alcoholism with some relevant issues relating to those studies. The present animal and human data suggest several alterations in the DA system in the context of alcoholism. Receptor studies imply that DA D(2) receptor density and function are lower at least among type 1 alcoholics, which suggests that they could benefit from drugs that enhance DAergic activity, such as partial DA agonists. These drugs could help to restore suboptimal levels of DAergic activity by reducing both the craving for alcohol in abstinence and the euphoria subsequent to alcohol’s release of DA in the nucleus accumbens (NAC), thus providing negative reinforcement for relapse.

Chronic alcoholics & White matter atrophy

* Cognitive impairment and diffuse white matter atrophy in alcoholics.

Authors: Mochizuki H, Masaki T, Matsushita S, Uwaga Y, Kamakura K, Arai H, Motoyoshi K, Higuchi S. - Department of Neurology, National Institute on Alcoholism, Kurilama National Hospital, Yokosuka, Kanagawa, Japan


Summary: OBJECTIVE: Diffuse brain white matter atrophy is often seen in chronic alcoholics, but its relation with cognitive impairment remains to be solved. In order to address this issue, in alcoholics with cognitive impairment at different levels, we studied relations of the central sensory conduction time (CSCT) or brain magnetic resonance imaging (MRI) findings with the cognitive function. METHODS: Subjects were 35 alcoholics with mild cognitive impairment (mini-mental state examination score, MMSE, >/=24; mean+/-SD, 27.7+/-1.9), 12 with moderate to severe cognitive impairment (MMSE<24; 20.3+/-2.7), 15 with Alzheimer's disease (AD) (MMSE, 19.9+/-4.3) (disease control) and 20 healthy volunteers (MMSE, 28.5+/-1.6) (normal control). Median nerve SEPs were recorded in the all subjects, and the latencies and amplitudes of their N9, N11, P13/14, N20 and P25 components were measured. The ventriculocranial ratio (VCR) and the width of cortical sulci were measured on MRIs. These physiological parameters and MRI findings were compared between the 4 groups of the subject, and correlations between those all features were also analyzed. RESULTS: CSCT and VCR were significantly greater in alcoholics with moderate to severe cognitive impairment than those in the other 3 groups. Pearson's product-moment correlation analyses of the alcoholics disclosed that both the CSCT and VCR had significant negative correlations with the MMSE score. Moreover, the CSCT and VCR were positively correlated. Conclusions: Both physiological and morphological estimates of the white matter function (CSCT and VCR) had a significant correlation with the cognitive dysfunction. SIGNIFICANCE: The diffuse white matter atrophy may be one of the factors causing cognitive impairment in chronic alcoholics.

ADHD & Opioid dependence

* History of attention-deficit hyperactivity disorder symptoms and opioid dependence: a controlled study.

Authors: Davids E, von Bunau V, Specka M, Fischer B, Scherbaum N, Gastpar M. - Department of Psychiatry and Psychotherapy, University of Duisburg-Essen, Ruhr Clinics Essen, Vorchowstr. 174, 45147 Essen, Germany.


Summary: The co-occurrence of attention-deficit hyperactivity disorder (ADHD) and substance use disorders has received considerable attention in recent clinical and scientific investigations. These two disorders are linked to one another in a variety of ways. The core symptoms of ADHD may be...
mimicked by the effects of psychoactive substance use, making it difficult to diagnose one disorder in the presence of the other. Individuals with ADHD may demonstrate earlier onset of the substance abuse and a pattern of more frequent or intense use. ADHD symptoms were explored as possible antecedents of opioid dependence. A total of 109 adult opioid-dependent, treatment-seeking male and female outpatients were investigated with an extended clinical semistructured interview to collect sociodemographic, drug-related, and clinical data. The results indicate that ADHD alone does not predispose the development of opioid dependence in our sample. Childhood ADHD symptoms may nevertheless be found more frequently related to school performance problems and difficulties in social adaptation, which was identified in more than half of our population. Patients with ADHD history seemed to experience a drug abuse career with more complications which need to be recognized with focused attention in order to start earlier treatment strategies.

SCL & Executive / Attentional Functions

* Impairments of executive / attentional functions in schizophrenia with primary and secondary negative symptoms.

**Authors:** Brazo P, Delamilleur P, Morello R, Halbecq I, Marie RM, Dollfus S. - Centre Esquirol, Centre Hospitalier Universitaire (CHU), Avenue Cote de Nacre, 14033 Caen, France; Groupe d'Imagerie Neurofonctionnelle, UMR 6095, CNRS/CEA/Universite de Caen/Universite de Paris V, Centre Cytceron, Boulevard Henri Becquerel, 14000 Caen, France.

**Source:** Psychiatry Res. 2005 Jan;30:133(1):45-55. Related Articles, Links

**Summary:** Frontal cognitive inabilities have been amply described in schizophrenic patients with negative symptoms, but findings are controversial. These discrepancies could be due to the fact that negative symptoms are heterogeneous, composed of primary and secondary negative symptoms. The hypothesis tested was that executive/attentional dysfunctions would be significantly more impaired in patients with primary than in patients with secondary negative symptoms independently of IQ, the severity of negative or positive symptoms, treatments and side effects. Fifty-six DSM-IV schizophrenic patients characterized either by primary or secondary negative symptoms and 56 controls matched on age, sex and level of education were assessed with executive/attentional cognitive tests. The categories score of the Modified Card Sorting Test (MCST) and the Verbal Fluency Test, which reflect solving and organizing skills, were significantly more impaired in the primary negative subtype than in the secondary negative subtype. In contrast, scores on the MCST (perseveration), the Trail Making Test and the Stroop Color Word Test, which test the ability to inhibit an automatic response, did not differ between the two subtypes. Conclusion: this study supports the view that primary and secondary negative symptoms could be associated with different levels of executive/attentional dysfunctions.

ADHD & WM deficits

* Computerized Training of Working Memory in Children With ADHD-A Randomized, Controlled Trial.

**Authors:** Klingberg T, Fernell E, Olesen PJ, Johnson M, Gustafsson P, Dahlstrom K, Gillberg CG, Forssberg H, Westerberg H.- Drs. Klingberg, Fernell, Forssberg, and Westerberg and Ms. Olesen are with the Unit of Neuropediatrics, Department Women and Children’s Health, Karolinska Institute, Stockholm Institute, Stockholm; Drs. Johnson and Gillberg are with the Department of Child and Adolescent Psychiatry, Goteborg University, Sweden; Dr. Gustafsson is with the Division of Child and Adolescent Psychiatry, Faculty of Health Sciences, Linkoping University, Sweden; Dr. Dahlstrom is with the Department of Neuropediatrics, Huddinge University Hospital, Sweden.

**Source:** J Am Acad Child Adolesc Psychiatry. 2005 Feb;44(2):177-186. Related Articles, Links

**Summary:** Objective: Deficits in executive functioning, including working memory (WM) deficits, have been suggested to be important in attention-deficit/hyperactivity disorder (ADHD). During 2002 to 2003, the authors conducted a multicenter, randomized, double-blind trial to investigate the effect of improving WM by computerized, systematic practice of WM tasks. METHOD: Included in the trial were 53 children with ADHD (9 girls; 15 of 53 inattentive subtype), aged 7 to 12 years, without stimulant medication. The compliance criterion (>20 days of training) was met by 44 subjects, 42 of whom were also evaluated at follow-up 3 months later. Participants were randomly assigned to use either the treatment computer program for training WM or a comparison program. The main outcome measure was the span-board task, a visuospatial WM task that was not part of the training program. RESULTS: For the span-board task, there was a significant treatment effect both post-intervention and at follow-up. In addition, there were significant effects for secondary outcome tasks measuring verbal WM, response inhibition, and complex reasoning. Parent ratings showed significant reduction in symptoms of inattention and hyperactivity/impulsivity, both post-intervention and at follow-up. Conclusions: This study shows that WM can be improved by training in children with ADHD. This training also improved response inhibition and reasoning and resulted in a reduction of the parent-rated inattentive symptoms of ADHD.

Pregnancy & Newer Antidepressants

**The safety of newer antidepressants in pregnancy and breastfeeding.**

**Authors:** Gentile S. - Department of Mental Health ASL Salerno 1, District n. 4, Cava de’ Tirreni (Salerno), Italy

**Source:** Drug Saf. 2005;28(2):137-52. Related Articles, Links

**Summary:** The pregnancy and postpartum periods are considered to be relatively high risk times for depressive episodes in women, particularly for those with pre-existing psychiatric illnesses. Therefore, it may be necessary to start or continue the pharmacological treatment of depression during these two timeframes. Hence, the aim of this review is to examine the effects on the fetus and infant of exposure, through the placenta and maternal milk, to the following drugs: fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram, mirtazapine, venlafaxine, reboxetine and bupropion. The teratogenic risks, perinatal toxicity and effects on the neurobehavioural development of newborns associated with exposure through the placenta or maternal milk to these medications need to be carefully assessed before starting psychopharmacological treatment in pregnant or lactating women. In spite of the limitations of some of the studies reviewed, the older selective serotonin-reuptake inhibitors (SSRIs) [as we await further data regarding escitalopram] and...
venlafaxine seem to be devoid of teratogenic risks. By contrast, the data concerning possible consequences related to exposure to SSRIs via the placenta and breastmilk on neonatal adaptation and long-term neurocognitive infant’s development are still controversial. Nevertheless, a number of reports have shown that an association between placental exposure to SSRIs and adverse but self-limiting effects on neonatal adaptation may exist. In addition, the information on both teratogenic and functional teratogenic risks associated with exposure to bupropion, mirtazapine and reboxetine is incomplete or absent; at present, these compounds should not be used as first-line agents in the pharmacological treatment of depression in pregnancy and breastfeeding. Untreated depression is not without its own risks since mothers affected by depression have a negative impact on the emotional development of their children and major depression, especially when complicated by a delusional component, may lead to the mother attempting suicide and infanticide. Consequently, clinicians need to help mothers weigh the risks of prenatal exposure to drugs for their babies against the potential risks of untreated depression and abrupt discontinuation of pharmacological treatment. Given these situations, we suggest that choosing to administer psychopharmacological treatment in pregnant or breastfeeding women with depression will result primarily from a careful evaluation of their psychopathological condition; currently, the degree of severity of maternal disease appears to represent the most relevant parameter to take this clinical decision.

PPD & Surveillance

- The onset of postpartum depression: Implications for clinical screening in obstetrical and primary care.

Authors: Stowe ZN, Hostetter AL, Newport DJ.
Summary: Objective Inconsistent diagnostic criteria fail to delineate guidelines for postpartum depression surveillance. This study evaluates the validity of commonly accepted postpartum onset criteria. Study design Consecutive referrals to the Emory Women’s Mental Health Program for evaluation of postpartum depression fulfilling criteria for major depression and taking no psychotropic medication were included. Diagnostic interview, demographics, depression scales, and the time of illness onset were obtained. Descriptive analysis was conducted for 3 participant groups: pregnancy onset, early postpartum onset within 6 weeks of delivery, and late postpartum onset. Results Among participants, 11.5% reported prenatal onset, 22.0% late postpartum onset, and 66.5% early postpartum symptom onset. Those reporting pregnancy onset were more likely to be unmarried, and those with a late postpartum onset were less likely to report a past history of postpartum depression. Conclusion The perinatal vulnerability to depression begins before delivery and extends beyond 6 weeks postpartum. Depression surveillance is therefore warranted during prenatal visits, at the postnatal check up, and at pediatric visits during the initial 6 months of the first postnatal year.

Pregnancy & Psychotropic disorders

- Psychotropic drugs in pregnancy: A case-control study.

Authors: Yarış F, Uluç K, Kesim M, Kadioglu M, Unsal M, Dikici MF, Kalyoncu NI, Yarış E. - Karadeniz Technical University, School of Medicine, Department of Family Medicine TR-61187, Trabzon, Turkey.
Summary: Psychotropic drug exposure during pregnancy is a common problem. Among the 601 cases exposed to drugs during pregnancy, who were followed by our Toxicology Information and Follow-up Service, 124 cases had used psychotropic drugs for depression, anxiety, or psychotic disorders. As the control group, 248 women, who did not use any drugs were selected. Of the 124 cases, 80 (64.5%) had healthy babies, and 17 (13.7%) decided to terminate the pregnancy. Spontaneous abortions, intrauterine death (in the 38th week) and premature deliveries were observed in the 9 (7.3%), 1 (0.8%) and 3 (2.4%) cases, respectively, in the drug exposure group. Pregnancies of the 14 (11.3%) cases were...
continuing during the preparation of this manuscript. Of the 248 controls, 151 (60.9%) had healthy babies, 9 (3.6%) experienced spontaneous abortion and 3 (1.2%) decided to terminate their pregnancies, 3 (1.2%) had premature deliveries, and we observed one (0.4%) congenital abnormality, 81 (32.7%) cases were still pregnant. Odds Ratio (95% confidence interval) for spontaneous abortion was found to be 1.35 (1.27-11.02) in the cases exposed to psychotropic drugs (P=0.02). No developmental problems were observed in the babies followed for 12 months. These data may give information about the early but not the late-term effects of psychotropic drugs used in pregnant women.

**Alzheimer disease**

**Dementia, Olanzapine, Risperidone & Anticholinergic activity**

- **Correlates of Anticholinergic Activity in Patients With Dementia and Psychosis Treated With Risperidone or Olanzapine.**

**Authors:** Mulsant BH, Gharamawi GM, Bossie CA, Mao L, Martinez RA, Tune LE, Greenspan AJ, Bastean JN, Pollock BG.

- From Western Psychiatric Institute and Clinic, Department of Psychiatry, Division of Geriatric Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pa. (Drs. Mulsant and Pollock); Janssen Medical Affairs, L.L.C., Titusville, N.J. (Drs. Gharamawi, Bossie, Greenspan, and Bastean and Mr. Mao); Geriatric Research, Education, and Clinical Center, Pittsburgh Veterans Administration Health System, Pittsburgh, Pa. (Dr. Mulsant); Janssen Research Foundation, Titusville, N.J. (Dr. Martinez); and Wesley Woods Health Center of Emory University, Atlanta, Ga. (Dr. Tune).

**Source:** J Clin Psychiatry. 2004 Dec;65(12):1708-1714. Related Articles, Links

**Summary:** Background: Older individuals with dementia are highly sensitive to the effects of muscarinic receptor blockade. Study Design: This was a 6-week multisite, randomized clinical trial. Subjects: Eighty-six patients with probable Alzheimer’s disease, vascular dementia, or mixed-etiolo gic dementia (DSM-IV criteria) were randomly assigned to treatment with olanzapine or risperidone. Assessments: Anticholinergic activity was measured with a radioreceptor assay, and plasma levels of antipsychotic medications were determined. Primary outcomes were assessed with the Udvalg for Kliniske Undersogelser (UKU) scale and somnolence adverse events; secondary outcome measures included scores on the Neuropsychiatric Inventory (NPI) and other scales. Results: There were no between-treatment differences in the UKU scale or in somnolence adverse events. Statistically significant improvements (p < .001) from baseline were found for the NPI measures, with no between-treatment group differences. Olanzapine was associated with significant increases from baseline in anticholinergic activity, while risperidone was not; the between-treatment group differences were not statistically significant. Increase in anticholinergic activity was associated with an increase in anticholinergic side effects and slower performance on the Trail Making Test Part A. Higher endpoint anticholinergic activity was associated with higher endpoint scores on several items from the NPI, including delusions, anxiety, and aberrant motor behavior. Implications: Efficacious doses of olanzapine increased anticholinergic activity in older patients with dementia, while similarly efficacious doses of risperidone did not. Patients whose anticholinergic activity increased were more likely to experience anticholinergic side effects and to have worsening in certain cognitive domains. These data suggest that certain patients may be vulnerable to the anticholinergic activity associated with antipsychotic treatment.

**Vitamin B12 deficiency & Reversible dementia**

- **Neuropsychology of vitamin B12 deficiency in elderly dementia patients and control subjects.**

**Authors:** Osimani A, Berger A, Friedman J, Porat-Katz BS, Abarbanel JM. - Kaplan Hospital, Rehovot, Israel and the Department of Behavioral Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel


**Summary:** Cobalamin deficiency may cause cognitive deficits and even dementia. In Alzheimer’s disease, the most frequent cause of dementia in elderly persons, low serum levels of vitamin B(12), may be misleading. The aim of this work was to characterize the cognitive pattern of B(12) deficiency and to compare it with that of Alzheimer’s disease. Nineteen patients with low levels of vitamin B(12) were neuropsychologically evaluated before treatment and a year later. Results were compared with those of 10 healthy control subjects. Final results suggest that there is a different pattern in both diseases. Twelve elderly patients with dementia improved with treatment. Seven elderly demented patients did not improve; they deteriorated after 1 year although their levels of cobalamin were normal. Analysis of the initial evaluation showed that the 2 groups of patients had a different neuropsychological profile. The group that improved had initially more psychotic problems and more deficits in concentration, visuospatial performance, and executive functions. They did not show language problems and ideomotor apraxia, which were present in the second group. Their memory pattern was also different. These findings suggest that cobalamin deficiency may cause a reversible dementia in elderly patients. This dementia may be differentiated from that of Alzheimer’s disease by a thorough neuropsychological evaluation.

**VaD & Nimodipine**

- **Efficacy and Safety of Nimodipine in Subcortical Vascular Dementia: A Randomized Placebo-Controlled Trial.**

**Authors:** Pantoni L, Del Ser T, Soglian AG, Amigoni S, Spadari G, Binelli D, Inzitari D. - From the Department of Neurological and Psychiatric Sciences, University of Florence, Florence, Italy; Section of Neurology, Hospital Severo Ochoa. Leganes, Madrid, Spain; Bayer SpA, Medical Department, Milan, Italy; and Opis Data Srl, Desio, Milan, Italy

**Source:** Stroke. 2005 Feb 3; [Epub ahead of print] Related Articles, Links

**Summary:** BACKGROUND AND PURPOSE: Evidence of drug efficacy in vascular dementia (VaD) is scanty. Therapeutic trials should address VaD subtypes. We studied the efficacy and safety of the calcium antagonist nimodipine in subcortical VaD. METHODS: 242 patients defined as affected by subcortical VaD based on clinical (ICD-10) and computed tomography criteria were randomized to oral nimodipine 90 mg/d or placebo.

**Arabpsynet e-Journal: Nº6 - April - May - June 2005**
RESULTS: 230 patients (121 nimodipine, mean age 75.2+/−6.1; 109 placebo, 75.4+/−6.0) were valid for the intention-to-treat analysis. At 52 weeks, the Sandoz Clinical Assessment Geriatric scale 5-point variation (primary outcome measure) did not differ significantly between the 2 groups. However, patients on nimodipine performed better than placebo patients in lexical production (P<0.01) and less frequently showed deterioration (3 or more point-drop versus baseline) on a Mini-Mental State Examination (28.1% versus 50.5%; chi(2) P<0.01) and Global Deterioration Scale (P<0.05). Dropouts and adverse events were all significantly more common among placebo than nimodipine patients, particularly cardiovascular (30 versus 13; RR, 2.26; 95% CI, 1.11 to 4.60) and cerebrovascular events (28 versus 10; RR, 2.48; 95% CI, 1.23 to 4.98), and behavioral disturbances requiring intervention (22 versus 5; RR, 3.88; 95% CI, 1.49 to 10.12). A worst-rank analysis, performed to correct for the effect of the high dropout rate in the placebo group, showed additional significant differences in favor of nimodipine in Set Test and MMSE total scores. Conclusions: Nimodipine may be of some benefit in subcortical VaD. Confirming previous results, the safety analysis of this study shows that in this high-risk population, nimodipine might protect against cardiovascular comorbidities.

**Agitated depression: a valid depression subtype?**

**Authors:** Benazzi F, E. Hecker Outpatient Psychiatry Center, Ravenna, Italy. F.Benazzi@fo.nettuno.it

**Source:** Prog Neuropsychopharmacol Biol Psychiatry, 2004 Dec;28(8):1279-85. Related Articles, Links

**Summary:** PURPOSE: The diagnostic validity of agitated depression (AD, a major depressive episode (MDE) with psychomotor agitation) is unclear. It is not classified in DSM-IV and ICD-10 classification of mental and behavioural disorder (ICD-10). Some data support its subtyping. This study aims to test the subtyping of AD. METHODS: Consecutive 245 bipolar-II (BP-II) and 189 major depressive disorder (MDD) non-tertiary-care MDE outpatients were interviewed (off psychoactive drugs) with Structured Clinical Interview for DSM-IV Axis I Disorders--Clinician Version (SCID-CV), Hypomania Interview Guide (HIGH-C), and Family History Screen. Intra-MDE hypomanic symptoms were systematically assessed. AD was defined as an MDE with psychomotor agitation. Mixed AD was defined as an MDE with four or more hypomanic symptoms (including agitation). FINDINGS: AD was present in 34.7% of patients. AD was mixed in 70.1% of AD patients. AD, vs. non-AD, had significantly (at alpha = 0.05) lower age at onset, more BP-II, females, atypical depressions, bipolar-I (BP-I) and BP-II family history, and was more mixed; racing/crowded thoughts, irritability, more talkativeness, and risky behaviour were significantly more common. Mixed AD, vs. non-AD, had significantly (at alpha = 0.01) lower age at onset, more intra-MDE hypomanic symptoms, BP-II, females, atypical depressions, BP-II family history, and specific hypomanic symptoms (distractibility, racing thoughts, irritable mood, more talkativeness, risky activities). Mixed AD, vs. non-mixed AD, had significantly more intra-MDE hypomanic symptoms (by definition), more recurrences, and more specific hypomanic symptoms (by definition). Non-mixed AD, vs. non-AD, had significantly more intra-MDE hypomanic symptoms and more talkativeness. Conclusions: AD was common in non-tertiary-care depression outpatients, supporting its diagnostic utility. AD and many bipolar diagnostic validators were associated, supporting its link with the bipolar spectrum. Mixed AD, but not non-mixed AD, had differences vs. non-AD similar to those of AD, suggesting that psychomotor agitation by itself may not be enough to identify AD as a subtype. Findings seem to support the subtyping of mixed AD. This subtyping may have important treatment impact, as antidepressants alone might increase agitation.

**Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence.**

**Authors:** Sink KM, Holden KF, Yaffe K - Sticht Center on Aging, Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA. kmsink@wfubmc.edu

**Source:** JAMA. 2005 Feb 2;293(5):596-608. Related Articles, Links

**Summary:** CONTEXT: Neuropsychiatric symptoms of dementia are common and associated with poor outcomes for patients and caregivers. Although nonpharmacological interventions should be the first line of treatment, a wide variety of pharmacological agents are used in the management of neuropsychiatric symptoms; therefore, concise, current, evidence-based recommendations are needed. OBJECTIVE: To evaluate the efficacy of pharmacological agents used in the treatment of neuropsychiatric symptoms of dementia. EVIDENCE ACQUISITION: A systematic review of English-language articles published from 1966 to July 2004 using MEDLINE, the Cochrane Database of Systematic Reviews, and a manual search of bibliographies was conducted. Inclusion criteria were double-blind, placebo-controlled, randomized controlled trials (RCTs) or meta-analyses of any drug therapy for patients with dementia that included neuropsychiatric outcomes. Trials reporting only depression outcomes were excluded. Data on the inclusion criteria, patients, methods, results, and quality of each study were independently abstracted. Twenty-nine articles met inclusion criteria. EVIDENCE SYNTHESIS: For typical antipsychotics, 2 meta-analyses and 2 RCTs were included. Generally, no difference among specific agents was found, efficacy was small at best, and adverse effects were common. Six RCTs with atypical antipsychotics were included; results showed modest, statistically significant efficacy of olanzapine and risperidone, with minimal adverse effects at lower doses. Atypical antipsychotics are associated with an increased risk of stroke. There have been no RCTs designed to directly compare the efficacy of typical and atypical antipsychotics. Five trials of antidepressants were included; results showed no efficacy for treating neuropsychiatric symptoms other than depression, with the exception of 1 study of citalopram. For mood stabilizers, 3 RCTs investigating valproate showed no efficacy. Two small RCTs of carbamazepine had conflicting results. Two meta-analyses and 6 RCTs of cholinesterase inhibitors generally showed small, although statistically significant, efficacy. Two RCTs of memantine also had conflicting results for treatment of caregivers. Although nonpharmacological interventions should be the first line of treatment, a wide variety of pharmacological agents are used in the management of neuropsychiatric symptoms of dementia. Of the agents reviewed, the atypical antipsychotics risperidone and olanzapine currently have the best evidence for efficacy. However, the effects are modest and further complicated by an increased risk of stroke. Additional trials of cholinesterase inhibitors enrolling patients with high levels of neuropsychiatric symptoms may be warranted.
impairs daytime functioning. Aim: To determine whether treatment with a proton-pump inhibitor (rabeprazole) would improve both objective and subjective measures of sleep. Methods: Individuals with complaints of significant gastro-oesophageal reflux disease were studied by polysomnography and 24-h pH monitoring on two separate nights. On one occasion, participants received 20 mg rabeprazole b.d., and on another, they received placebo. Both study conditions were preceded by a week of treatment with either rabeprazole or placebo. The order of treatments was randomized. Results: Rabeprazole significantly reduced overall acid reflux, but it did not significantly reduce night-time acid contact. Rabeprazole treatment significantly improved subjective indices of sleep quality. There were no significant differences on objective measures of sleep between placebo and rabeprazole treatment. Conclusions: Consistent with other studies of pharmacological treatments for gastro-oesophageal reflux, subjective measures of sleep improved with heartburn medication but objective measures were not affected.

* Nefazodone in primary insomnia:
  an open pilot study.

Authors: Wiegand MH, Galanakis P, Schreiner R. - Department of Psychiatry and Psychotherapy, Technical University of Munich, Ismaninger Str. 22, D-81675 Munich, Germany. mhwiegand@lrz.tum.de


Summary: The present study is the first to investigate the effect of the antidepressant nefazodone on sleep in patients with primary (psychophysiological) insomnia. Following baseline assessment of sleep (polysomnography and subjective sleep parameters), 32 patients received initially 100 mg nefazodone in a single dose at bedtime; according to efficacy and tolerability, the dose could be increased up to 400 mg. Polysomnography and assessment of subjective sleep parameters were repeated after 4 weeks’ administration. 12 patients dropped out, 11 of them due to lack of efficiency or intolerable side effects. In 20 patients who completed, the authors observed a lengthened sleep onset latency, decreases in stage 1 and slow wave sleep, and increases in stages 2 and REM under nefazodone. Subjective measures of sleep mirrored a clearer improvement: there was a significant reduction of the PSQI total score and all subscores except sleep latency. We suppose that the dose range chosen was too high for this patient population, thus accounting for the high proportion of dropouts and the partly unfavorable effects on objective sleep parameters. For a definite evaluation of the possible role of nefazodone in the treatment of primary (psychophysiological) insomnia, double-blind, placebo-controlled, randomized studies with lower doses are needed.

### Sleep quality & GIR

#### SD & AD

* Sleep disorders in Alzheimer's disease and other dementias.

Authors: Blwise DL. - Department of Neurology, Program in Sleep, Aging and Chronobiology, Emory University Medical School, Atlanta, Georgia 30328, USA.


Summary: Patients with dementias, such as Alzheimer's disease (AD), often have nocturnally disrupted sleep. Clinically,
this may present as agitation during the nighttime hours, which may affect as many as a quarter of AD patients during some stage of their illness. Sleep disturbance in AD may be multifactorial and involve sleep-disordered breathing and disrupted chronobiology, both often characterized by excessive daytime napping. Polysomnographically, AD patients show decreased rapid eye movement (REM) sleep in proportion to the extent of their dementia: some evidence suggests that cholinesterase inhibitors, commonly used pharmacologic agents for cognitive loss in AD, may increase REM sleep measures. Unfortunately, such agents may also induce insomnia and vivid dreams. There have been no randomized clinical trials of sedative-hypnotic medications specifically targeted at AD patients with sleep problems. Evidence suggests that sedative-hypnotics, such as benzodiazepine site-specific agonists, may have a role in some cases, whereas atypical antipsychotics may be necessary in others. There are also reports of successful interventions with nonpharmacologic options (eg, exercise, illumination). The utility of melatonin as a hypnotic in this population appears equivocal.

Sleep disorders

* Sleep disorders: an overview.

**Authors:** Roehrs T, Roth T. - Sleep Disorders and Research Center, Henry Ford Hospital, Department of Psychiatry and Behavioral Neurosciences Wayne State University School of Medicine, Detroit, Michigan 48202, USA.

**Source:** Clin Cornerstone. 2004;6 Suppl 1C:S6-16. Related Articles, Links

**Summary:** Although sleep disorders medicine is a relatively young discipline, understanding of the diagnosis, pathophysiology, and treatment of sleep disorders is evolving at a rapid pace. This overview discusses the history of the development of sleep disorders medicine, tracing changes in the diagnostic classification of sleep disorders as well as the role of polysomnography in diagnosis. This evolution is most evident for insomnia, one of the major sleep disturbances. The accumulation of epidemiologic data on the prevalence and temporal course of insomnia and emerging information regarding its pathophysiology derived from laboratory assessments have led to the development of new therapeutic approaches for primary insomnia and insomnia associated with medical and psychiatric disorders.

SD & PD

* Sleep disorders in Parkinson's disease.

**Authors:** Thorpy MJ. - Sleep-Wake Disorders Center, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA.

**Source:** Clin Cornerstone. 2004;6 Suppl 1A:S7-15. Related Articles, Links

**Summary:** Depression, dementia, and physiologic changes contribute to the high prevalence of sleep disturbances in patients with Parkinson's disease (PD). Antiparkinsonian drugs also play a role in insomnia by increasing daytime sleepiness and affecting motor symptoms and depression. Common types of sleep disturbances in PD patients include nocturnal sleep disruption and excessive daytime sleepiness, restless legs syndrome, rapid eye movement sleep behavior disorder, sleep apnea, sleep walking and sleep talking, nightmares, sleep terrors, and panic attacks. A thorough assessment should include complete medical and psychiatric histories, sleep history, and a 1 to 2-week sleep diary or Epworth Sleepiness Scale evaluation. Polysomnography or actigraphy may also be indicated. Treatment should address underlying factors such as depression or anxiety. Hypnotic therapy for sleep disturbances in PD patients should be approached with care because of the risks of falling, agitation, drowsiness, and hypotension. Behavioral interventions may also be useful.

SD, Women & BZRs

* Women and insomnia.

**Authors:** Miller EH. - Albert Einstein College of Medicine, New York, USA. EhMiller@nshs.edu

**Source:** Clin Cornerstone. 2004;6 Suppl 1B:S8-18. Related Articles, Links

**Summary:** The occurrence of insomnia in women is influenced in great part by the complex hormonal cycles they undergo. Patterns of insomnia in younger women may be physiologically different on a hormonal basis from those found in older women. Although significant objective sleep disturbances have been difficult to demonstrate across the menstrual cycle in normal women, the International Classification of Sleep Disorders (ICSD) includes premenstrual insomnia and premenstrual hypersomnia as sleep disorders within the category of menstrual-associated sleep disorder. On the other hand, during pregnancy and after childbirth, profound fluctuations in steroid and hypothalamic-pituitary-adrenal axis-related hormones produce significant physiological changes, including sleep disruption. During the menopausal transition, significant sleep disruptions are provoked by sleep-disordered breathing, vasomotor disturbance, and mood disorders. Regardless of age, women with chronic insomnia are at higher risk for developing or sustaining depression. Thoughtful management approaches must consider known relationships between menstrual or menopausal status and various sleep disorders, and should rely on pharmacologic, nonpharmacologic, or a combination of treatments to achieve successful relief from insomnia. The off-label, first-line use of antipressants for treating insomnia in the absence of depression is now considered debatable. The long-term efficacy and safety of the newer benzodiazepine receptor agonists (BZRs) for insomnia, whether taken nightly or episodically, are supported by existing clinical experience. US Food and Drug Administration guidelines limiting the use of hypnotics to only a few weeks predate the newer generation BZRs, and, as such, the guidelines may no longer be truly appropriate for these new agents.

SD, Insomnia & Women

* Depression and insomnia in women.

**Authors:** Krystal AD. - Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, North Carolina 27710, USA. Kryst001@mc.duke.edu

**Source:** Clin Cornerstone. 2004;6 Suppl 1B:S19-28. Related Articles, Links

**Summary:** Depressions and insomnia are both significantly more prevalent in women than in men. Risks appear linked to fluctuations and transitions in gonadal hormones during various phases of women's lives, with the risk of depression greatest during the period from menarche to menopause. Increased risks of both insomnia and depression also coincide with the late luteal phase of the menstrual cycle, during and after pregnancy, and during the peri-/postmenopausal period. Gonadal hormones exert significant effects on the neurohumoral systems most intimately associated with depression and insomnia, with corresponding implications for treatment. Medications related to...
Chronic insomnia

- Chronic insomnia: current issues.

Authors: Neubauer DN. - The Johns Hopkins School of Medicine, Department of Psychiatry, The Johns Hopkins Sleep Disorders Center, Baltimore, Maryland 21224, USA. neubauer@jhmi.edu


Summary: Insomnia is a common problem in the general population and has a higher prevalence in persons with medical and psychiatric disorders. Although insomnia is most often transient, occurring as a result of identifiable stressors, a substantial portion of insomnia cases involve persistent sleep difficulty. This chronic form of insomnia may be associated with a wide range of adverse consequences. An understanding of the characteristics and causes of this disorder and the available therapeutic strategies will promote more effective identification and treatment of patients with chronic insomnia.

Cosleeping & Solitary - sleeping infants

- A comparison of the sleep-wake patterns of cosleeping and solitary-sleeping infants.

Authors: Mao A, Burnham MM, Goodlin-Jones BL, Gaylor EE, Anders TF. - George Washington University, USA


Summary: This study examined whether 3-15 month-old cosleeping infants displayed differences in time spent in active versus quiet sleep, and in the number/duration of nighttime awakenings when compared with solitary-sleeping infants; and also whether they spent the majority of the night sleeping face-to-face, as previously reported. Nine cosleeping and nine solitary-sleeping infants were matched on age, gender, ethnicity, maternal age, and family SES. Video recordings of nighttime sleep yielded percentage of time in active sleep, quiet sleep, and awake, number of awakenings, and the percentage of time cosleeping infants and mothers spent face-to-face. Across age, cosleeping infants had more awakenings per night mean 5.8(1.50) versus 3.2(1.95); t = 3.16, p = .006). The percent of the nighttime spent awake did not differ between groups, suggesting that cosleeping infants had shorter awakenings. Cosleeping infants spent 40% of the night face-to-face with their mothers.

PD, Sleep & daytime sleepiness

- Sleep and daytime sleepiness with Parkinson's disease before and after dopaminergic treatment.

Authors: Kaynak D, Kiziltan G, Kaynak H, Benbir G, Uysal O. - Department of Neurology, Cerrahpaşa Faculty of Medicine, Istanbul University, Istanbul, Turkey.


Summary: Sleep disturbances and daytime sleepiness are well-known phenomena in Parkinson's disease (PD). Fifteen previously untreated PD patients underwent clinical evaluation, subjective sleep evaluation and polysonomographic evaluation (PSG) before and after a treatment period of mean 8 +/- 3.1 months with dopaminergic drugs. Both mean Unified Parkinson's Disease Rating Scale (UPDRS) total score and mean subset III of the UPDRS were significantly improved with dopaminergic treatment. PSG revealed that administration of dopaminergic drugs resulted in significant increase in mean percentage of stages 1 and 2. The mean Epworth Sleepiness Scale (ESS) score was significantly increased and mean Multiple Sleep Latency Test (MSLT) score was significantly decreased after dopaminergic treatment indicating subjective and objective daytime sleepiness. The differences in MSLT scores were best explained by a higher dose of l-dopa, whereas other variables such as disease duration, treatment duration, Hoehn and Yahr stage, sleep efficiency index or dopamine agonists did not increase the significance. In contrast, any of the variables appeared to explain ESS score variability. This study demonstrates that daytime sleepiness is not present in untreated patients but emerges later during dopaminergic treatment. Total daily l-dopa dose is predictive of objective daytime sleepiness. Furthermore, subjective assessment of sleepiness may cause underestimation of the severity of daytime sleepiness.

Addiction disorders

Rapid delivery of drugs & Addiction

- Why does the rapid delivery of drugs to the brain promote addiction?

Authors: Samaha AN, Robinson TE. - Department of Psychology (Biopsychology Program), University of Michigan, Ann Arbor, MI 48109-1109, USA


Summary: It is widely accepted that the more rapidly drugs of abuse reach the brain the greater their potential for addiction. This might be one reason why cocaine and nicotine are more addictive when they are smoked than when they are administered by other routes. Traditionally, rapidly administered drugs are thought to be more addictive because they are more euphorogenic and/or more reinforcing. However, evidence for this is not compelling. We propose an alternative (although not mutually exclusive) explanation based on the idea that the transition to addiction involves drug-induced plasticity in mesocorticolimbic systems, changes that are manifested behaviourally as psychomotor and incentive sensitization. Recent evidence suggests that rapidly administered cocaine or nicotine preferentially engage mesocorticolimbic circuits, and more readily induce psychomotor sensitization. We conclude that rapidly delivered drugs might promote addiction by promoting forms of neurobehavioural plasticity that contribute to the compulsive pursuit of drugs.
**Psychiatric New Papers**

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**Escitalopram / Reboxetine, MDD & SUD**

- Escitalopram/reboxetine combination in depressed patients with substance use disorder.

**Authors**: Camarasa X, Lopez-Martinez E, Duboc A, Khazaal Y, Zulino DF. - Hospital Psychiatric Canton of Mansens, Switzerland


**Summary**: Acting pharmacologically on different transmitter systems has been suggested to have some advantages in patients with substance abuse and may possibly address a larger spectrum of symptoms. One major drawback of using antidepressants addressing several neurotransmitters is that the relative activities on the different neurotransmitters cannot individually be adjusted. Combining antidepressants targeting different neurotransmitter systems may allow adapting the effect individually be adjusted. Combining antidepressants targeting different neurotransmitters cannot individually be adjusted. Combining antidepressants targeting different neurotransmitter systems may allow adapting the effect individually be adjusted.

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**DBT & Alcohol dependency**

- [Application of dialectical behavior therapy in in-patient treatment for alcohol dependency.] [Article in German]

**Authors**: Mayer-Bruns F, Lieb K, Dannegger E, Jacob GA. Rehaklinik Glockelhof, Schilchsee

**Source**: Nervenarzt. 2005 Feb 5; [Epub ahead of print] Related Articles, Links

**Summary**: Dialectical behavior therapy (DBT) was originally developed for suicidal female patients with borderline personality disorder (BPD). Meanwhile, DBT-based approaches to psychotherapy have also been successfully applied in other clinical groups. Previous studies of DBT in patients suffering from BPD and comorbid drug addiction are discussed, and an approach to DBT that has been devised by the authors for use in the treatment of alcoholics with comorbid BPD is described. As these patients have more severe clinical problems and less satisfactory treatment responses than do alcoholics without comorbid BPD, we must hope that this new approach will improve clinical outcomes in these severely ill patients.

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**Mirtazapine, Venlafaxine & Alcool detoxification**

- Mirtazapine and venlafaxine in the management of collateral psychopathology during alcohol detoxification.

**Authors**: Liappas J, Paparrigopoulos T, Tzavellas E, Rabavilas A. - Athens University Medical School, Department of Psychiatry, Eginition Hospital, 74 Vas. Sofias Ave., 115 28 Athens, Greece


**Summary**: Symptoms of anxiety and depression are common in a large proportion of alcohol-abusing/dependent individuals during alcohol detoxification. The aim of this study was to examine the impact of a combined psychotherapeutic-

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**Psychotropics drugs**

**Sexual Side Effects, Citalopram & Paroxetine**

- Incidence of Sexual Side Effects in Refractory Depression During Treatment With Citalopram or Paroxetine

**Authors**: Landen M, Hogberg P, Thase ME. - From the Section of Psychiatry St. Goran, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden (Dr. Landen); Bristol-Myers Squibb, Bromma, Sweden (Mr. Hogberg); the Department of Psychiatry, University of Pittsburgh Medical Center (Dr. Thase); and the Western Psychiatric Institute and Clinic (Dr. Thase), Pittsburgh, Pa.

**Summary**: OBJECTIVE: The incidence of sexual dysfunction due to antidepressant drugs reported in pre-marketing clinical efficacy trials is often several times lower than in subsequent clinical experiences and independent reports. Although it is commonly believed that the reason for this discrepancy is that the nonleading questions employed in conventional clinical trials underestimate sexual dysfunction while the direct questioning used in independent trials provides more accurate data, few studies have actually compared these 2 methods. METHOD: In this study, 119 patients with a DSM-IV-defined major depressive episode (82 women and 37 men) who had been treated with but not responded to a selective serotonin reuptake inhibitor (SSRI; either citalopram or paroxetine) were assessed regarding sexual function by means of open-ended questions and direct questioning at baseline (after SSRI treatment only) and after 4 weeks of SSRI treatment plus buspirone or placebo. RESULTS: More patients reported sexual dysfunction in response to direct questioning (41%) as compared with spontaneous report (6%) (p < .001). Sexual dysfunction correlated with the duration of the depressive episode, but not with age, dose of SSRI, plasma level of SSRI, duration of SSRI treatment, or any measurement of depression. No statistically significant differences regarding psychopharmacological (either with mirtazapine or venlafaxine) treatment of these symptoms during the early withdrawal phase of alcohol compared to a group treated only with psychotherapy. A total of 60 alcohol-dependent/abusing subjects randomly assigned to three groups (psychotherapy, psychotherapy plus mirtazapine, psychotherapy plus venlafaxine) were studied. Assessment of psychopathology and global functioning throughout a 4-5-week detoxification period was done by the Hamilton Anxiety Rating Scale (HARS), the Hamilton Depression Rating Scale (HDRS), and the Global Assessment Scale (GAS). At baseline, high scores of anxiety and depression were recorded (HARS: controls: 33.1+/-7.8, mirtazapine: 33.2+/-12.6, venlafaxine: 36.6+/-5.4; HDRS: controls: 39.5+/-7.4, mirtazapine: 37.9+/-7.8, venlafaxine: 41.9+/-4.5). A marked improvement (p<0.001) was evidenced in all groups by the end of the detoxification period. However, patients on mirtazapine improved significantly more compared to the other two groups (HARS: controls: 9.6+/-7.6, mirtazapine: 4.3+/-4.4, venlafaxine: 7.2+/-4.1, *p=0.011; HDRS: controls: 8.6+/-7.9, mirtazapine: 3.8+/-3.2, *p=0.017; GAS: controls: 79.5+/-9.4, mirtazapine: 87.5+/-5.5, *p=0.006). It is concluded that addition of mirtazapine, but not venlafaxine, to a standard psychotherapy-oriented alcohol detoxification treatment may facilitate the detoxification process by minimizing psychological discomfort. Consequently, it may prove to be a facilitator for the long-term abstinence from alcohol.
the incidence of sexual dysfunction were found between the citalopram and the paroxetine groups. Conclusion: Open-ended questions are an insufficient tool to estimate sexual dysfunction, and premarketing clinical trials should therefore include basic explicit assessments. The failure to find a correlation between treatment duration and sexual dysfunction adds to the notion that sexual side effects due to SSRIs do not abate over time.

**Clozapine & Cardiac Effects**

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**Adverse Cardiac Effects Associated With Clozapine.**

**Authors:** Merrill DB, Dec GW, Goff DC. - *New York State Psychiatric Institute, Department of Psychiatry, Columbia University, New York, NY; dagherHarvard Medical School and the Heart Failure and Transplantation Unit, Massachusetts General Hospital, Boston, MA and double dagherHarvard Medical School and the Psychiatry Service of the Massachusetts General Hospital, Boston, MA*


**Summary:** OBJECTIVE: To review the published literature on serious adverse cardiac events associated with the atypical antipsychotic agent, clozapine, and to make recommendations for cardiac assessment of candidates for clozapine treatment and for monitoring of cardiac status after treatment is initiated. DATA SOURCES: We searched the PubMed and MEDLINE databases for articles published from 1970 to 2004 that contain the keywords "clozapine and myocarditis," "clozapine and cardiomyopathy," "clozapine and cardiotoxicity," "clozapine and sudden death" or "clozapine and mortality." We also manually searched the bibliographies of these articles for related sources. STUDY SELECTION: We reviewed the 30 case reports, case series, laboratory and clinical trials, data mining studies, and previous reviews identified by this search. DATA SYNTHESIS: Recent evidence suggests that clozapine is associated with a low (0.015% to 0.188%) risk of potentially fatal myocarditis or cardiomyopathy. The drug is not known to be independently associated with pathologic prolongation of the QTc interval, but it may contribute to pathologic QTc prolongation in patients with other risk factors for this condition. Conclusions: The low risk of a serious adverse cardiac event should be outweighed by a reduction in suicide risk for most patients taking clozapine. We provide recommendations for assessing and monitoring cardiac status in patients prior to and after initiation of treatment with clozapine.

**Quality of life, Typical & Atypical antipsychotics**

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**[Clozapine, 10 years after - A Clinical Review] [Article in French]**

**Authors:** Llorca PM, Pere JJ. - CHU Gabriel Montpied, 58, rue Montalembert, 63000 Clermont Ferrand, France

**Source:** Encephale. 2004 Sep-Oct;30(5):474-91.

**Summary:** clozapine was one of the major advances in the treatment of schizophrenia since the introduction of the classic antipsychotic agent chlorpromazine in the 1950s. Over the past 10 years, clozapine has become the reference compound for the development of new antipsychotics, and new drugs have been developed which have also claimed atypical status. The indications of clozapine were recently extended to psychosis in Parkinson's disease and harmonized in the European Union. This provides the opportunity to update the data on clozapine in the treatment of schizophrenia. In this article we review current clinical evidence in schizophrenia to address the following issues: 1) Efficacy in refractory/positive symptoms: a systematic and critical analysis of 14 double-blind clinical trials in comparison with both standard and novel antipsychotics show consistent findings in favour of clozapine, with all but three of the reports demonstrating superiority. The review of studies allow us to say little about the predictors of treatment response, time to clozapine response and about the impact of clozapine on the quality of patients' life and longer-term outcome. Treatment options for clozapine non-responders are reviewed. 2) Risk of EPS: clozapine is considered to have a minimal risk of EPS and in all studies where a valid methodology was used, a clear superiority over the other neuroleptics is demonstrated. It is pointed out that, if the prevalence and incidence of EPS with clozapine is low, it is not zero. All the studies assessing clozapine treatment for TD have major methodological limitations, so no final conclusion can be drawn. 3) Efficacy for primary and secondary negative symptoms and neuropsychological effects: the data of clinical studies where negative symptoms scales were used favour clozapine in terms of improvement. However most of the studies were carried out in populations with predominantly positive symptoms. With regard to the need to distinguish primary and secondary symptoms, data are conflicting regarding the benefit of clozapine. Due to the lack of studies with a valid methodology, no definitive conclusion can be drawn about the efficacy on clozapine on the deficit syndrome and on neuropsychological disorders. 4) Impact on suicide risk: 4 out of 6 retrospective studies provide evidence for the ability of clozapine therapy to reduce suicidal behaviour. The results of a recent randomized, parallel-group study designed to compare clozapine versus olanzapine in preventing suicide attempts seems to confirm this hypothesis. We also address the tolerability and safety data, especially haematologic, comitial, cardiovascular and metabolic side-effects. The effectiveness of blood monitoring for the management of neutropenia and agranulocytosis demands that the recommendations are strictly followed. The use of clozapine at doses higher than 600 mg daily should follow published recommendations, in order to minimize the risk of seizures; these include anticonvulsant regimens based on blood levels. With regard to the cardiovascular mortality, if clozapine therapy has negligible effects on QT interval, its association with potential fatal myocarditis cannot be excluded in young patients who should be investigated if they develop cardiac symptoms in the first weeks of treatment. Available data support the notion that the frequency of bodyweight gain is high with several new antipsychotics, including clozapine. Potential long term effects of bodyweight gain on mortality and morbidity have to be taken into consideration. The pharmacological mechanisms underlying the "unique clozapine profile" is discussed. Clozapine remains the only antipsychotic with efficacy at relatively low D2 receptor occupancy. The pharmacogenetic and pharmacokinetic aspects are also reviewed. Finally, the place of clozapine in the current treatment of schizophrenia is highlighted to inform the development of guidelines for clinical management.

**Arabpsynet e-Journal: Nº 6 – April – May – June 2005**
METHOD: All patients, who suffer from schizophrenia and significant improvement in the positive and negative answer to the psychosocial rehabilitation intervention in terms of Residential Rehabilitation Centre; to examine whether the subjective well being with regard to the pharmacological exists a meaningful relation between quality of life and the study: 22 patients treated with atypical drugs and 10 with of psychosocial rehabilitation, we found a statistically meaningful symptomatology, subjective well-being and quality of life. From the statistical analysis of the data to the endpoint, after a month significant statistical difference at baseline with regard to typical. The analysis of the collected data didn't show any significant statistical difference at baseline with regard to symptomatology, subjective well-being and quality of life. From the statistical analysis of the data to the endpoint, after a month of psychosocial rehabilitation, we found a statistically meaningful improvement in all the areas inquired in the group of the patients dealt with antipsychotic atypical drugs. Conclusion: The results confirm that the atypical antipsychotics are more efficacy, than typical, to improve symptomatology, subjective well-being and quality of life of psychiatric patients.

Lamotrigine & Complex elderly patients

- Tolerability and effectiveness of lamotrigine in complex elderly patients.

Authors: Aulakh JS, Hawkins JW, Athwal HS, Sheikh JI, Yesavage J, Tinklenberg JR,- VA Palo Alto Health Care System and Mental Illness Research, Educational and Clinical Center and Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine


Summary: There is paucity of medical literature on the use of lamotrigine in elderly patients who have behavior problems and diverse psychiatric syndromes. This article is a retrospective case series summarizing the authors’ experience with this medication. In a 20-patient case series from an institutional review board-approved retrospective chart review, the tolerability and efficacy of lamotrigine was evaluated for the management of agitated and aggressive behaviors in nursing home patients with a range of psychiatric and medical diagnoses. Nineteen of the elderly nursing home patients tolerated lamotrigine treatment, and 18 showed modest clinical improvement. These results support the authors’ belief that controlled clinical investigations of this medication should be performed.

Severe delirium & Donepezil

- Severe delirium due to basal forebrain vascular lesion and efficacy of donepezil

Authors: Kobayashi K, Higashima M, Mutou K, Kidani T, Tachibana O, Yamashita J, Koshino Y. - Department of Psychiatry and Neurobiology, Kanazawa University Graduate School of Medical Sciences, 13-1, Takara-machi, Kanazawa, Ishikawa-kken, 920-8641, Japan. kobakatu@med.m.kanazawa-u.ac.jp


Summary: A severe intractable delirium caused by the basal forebrain vascular lesion and its dramatic recovery after donepezil administration were reported. A 68-year-old man had suffered for a month from delirium of mixed type caused by the right basal forebrain vascular lesion after surgery for craniopharyngioma. Magnetic resonance imaging (MRI) showed hemorrhagic infarcts in the head of the right caudate nucleus and the right basal forebrain of the medial septal nucleus, diagonal band of Broca and nucleus basalis of Meynert. He had been treated with anti-psychotics, anti-depressants and hypnotics, which resulted in little improvement. Donepezil administration dramatically improved his intractable delirium at the 19th post-donepezil administration day, but this was followed by amnestic symptoms. Clinical correlates of delirium with the basal forebrain lesion and efficacy of donepezil support the hypocholinergic theory of delirium.

Clozapine, Sleep, BD & SCZ

- Effects of clozapine on sleep in bipolar and schizoaffective disorders.

Authors: Armitage R, Cole D, Suppes T, Ozcan ME. Department of Psychiatry, Sleep Study Unit, The University of Texas Southwestern Medical Center, 2201 Inwood Road, Dallas, TX 75235, USA. Roseanne.Armitage@med.umich.edu


Summary: OBJECTIVE: Sleep disturbances are strongly associated with mood disorders, although the majority of data have been obtained in patients with major depressive disorder. Studies reporting results in bipolar disorder are few, and results have not been consistent. Clozapine is a prototype of atypical antipsychotics, which is effective in improving symptoms of manic episodes in patients with bipolar disorder, or schizoaffective disorder, bipolar type and has been shown to influence sleep in other psychiatric disorders. The present study evaluated the sleep effects of clozapine in bipolar and schizoaffective disorders. METHODS: Participants were 11 women and 4 men (range:28-53 years of age, mean 40.9+/−8.6 years), all with a history of mania by DSM-IV criteria for either bipolar I disorder or schizoaffective disorder, bipolar type. They participated in a sleep study at baseline and again after 6 months initiation of clozapine add-on therapy. RESULTS: Sleep latency was longer on clozapine and the number of awakenings were increased, whereas time in bed (TIB) and total sleep period (TSP) were increased (range: F=6.2-17.9; df=1,12; p<0.05). Although none of the individual sleep stage showed significant treatment changes, both Stage 2 and slow-wave sleep were increased and Stage 2 decreased on clozapine. Subjective sleep measures improved on clozapine with a small but significant improvement in how rested patients felt upon awakening (t=−2.1; df=26; p<0.05).

Conclusion: Clozapine prolonged sleep latency, improved restedness, and increased total sleep time. Although lack of a control group limits interpretation of these results, they are in general agreement with studies in other psychiatric populations, and support the view that clozapine is primarily a NREM sleep enhancer. The improvement in restedness may be of positive clinical consequence.
Conclusions:

Behaviour therapy presents more and more helpful treatment with clonidine and (from the group of novel literature and practical experience. RESULTS: Worldwide, drug of the art. METHOD: A critical review of the empirically based the progress in the field should be explored to find out the state of the art. BACKGROUND: Within the last decade therapeutic approaches to tic disorders are reflected in many new studies. The advent of novel neuroleptics and the more sophisticated behavioural techniques may give new hope to children and adolescents with tic disorders. OBJECTIVE: Hence, the progress in the field should be explored to find out the state of the art. METHOD: A critical review of the empirically based literature and practical experience. RESULTS: Worldwide, drug treatment with clonidine and (from the group of novel antipsychotics) risperidone show the broadest empirical basis while in Europe benzamides have a good empirical clinical background. Behaviour therapy presents more and more helpful empirical data.

Conclusions: Risperidone may become the first-line drug in treatment of tic disorders and behaviour therapy might be increasingly used within a multimodal treatment program.

Summary: Background: Benzodiazepine dependency can occur as a result of treatment for anxiety disorders or sleep disturbance. While benzodiazepine withdrawal can be challenging, cessation of use can be even more difficult if there are other comorbidities such as oestrogen deficiency with vasomotor symptoms and anxiety disorders. Objective: This article provides practical information for general practitioners in the management of patients with benzodiazepine dependency. Discussion: Some patients may have common medical presentations and coexisting drug dependence. It is often difficult to separate these two issues. In the case of benzodiazepine dependence, gradual withdrawal over time and nonpharmacological treatment of the symptoms of withdrawal such as anxiety or insomnia is effective. Better outcomes are achieved where the GP discusses and plans strategies with the patient. Treatment often involves multiple interventions from various health professionals. General practitioners are ideally placed to coordinate such treatment.

Summary: BACKGROUND: The last decade therapeutic approaches to tic disorders are reflected in many new studies. The advent of novel neuroleptics and the more sophisticated behavioural techniques may give new hope to children and adolescents with tic disorders. OBJECTIVE: Hence, the progress in the field should be explored to find out the state of the art. METHOD: A critical review of the empirically based literature and practical experience. RESULTS: Worldwide, drug treatment with clonidine and (from the group of novel antipsychotics) risperidone show the broadest empirical basis while in Europe benzamides have a good empirical clinical background. Behaviour therapy presents more and more helpful empirical data.

Conclusions: Risperidone may become the first-line drug in treatment of tic disorders and behaviour therapy might be increasingly used within a multimodal treatment program.
between diazepam equivalents and photo recognition. It was concluded that anterograde amnesia was strongly associated with benzodiazepines in patients who take benzodiazepines in an overdose. Sedation does not predict the degree of anterograde amnesia.

**Quetiapine & Cortical effects**

- **Cortical effects of quetiapine in first-episode schizophrenia: a preliminary functional magnetic resonance imaging study.**

  **Authors:** Strobel M, Warnke A, Roth M, Schulze U. - Klinik und Poliklinik für Kinder- und Jugendpsychiatrie und Psychotherapie der Julius-Maximilian-Universität Würzburg

  **Source:** Biol Psychiatry. 2004 Dec 15;56(12):938-42. Related Articles, Links

  **Summary:** BACKGROUND: Quetiapine improves both psychotic symptoms and cognitive function in schizophrenia. The neural basis of these actions is poorly understood. METHODS: Three subject groups underwent a single functional magnetic resonance imaging (fMRI) session: drug-naive (n = 7) and quetiapine-treated samples of patients with schizophrenia (n = 8) and a healthy control group (n = 8). The fMRI session included an overt verbal fluency task and a passive auditory stimulation task. RESULTS: In the verbal fluency task, there was significantly increased activation in the left inferior frontal cortex in the quetiapine-treated patients and the healthy control sample compared with the drug-naive sample. During auditory stimulation, the healthy control group and stably treated group produced significantly greater activation in the superior temporal gyrus than the drug-naive sample. Conclusions: Quetiapine treatment is associated with altered blood oxygen level-dependent responses in both the prefrontal and temporal cortex that cannot be accounted for by improved task performance subsequent to drug treatment.

**Paroxetine & Clomipramine in AN with DE**

- **[Paroxetine versus clomipramine in female adolescents suffering from anorexia nervosa and depressive episode—a retrospective study on tolerability, reasons for discontinuing the antidepressive treatment and different outcome measurements] [Article in German]**

  **Authors:** Strobel M, Warnke A, Roth M, Schulze U. - Klinik und Poliklinik für Kinder- und Jugendpsychiatrie und Psychotherapie der Julius-Maximilian-Universität Würzburg

  **Source:** Z Kinder Jugendpsychiatri Psychother. 2004 Nov;32(4):279-89. Related Articles, Links

  **Summary:** OBJECTIVES: So far, there have only been few studies concerning the question of indication and efficacy of antidepressive medication in children and adolescents with anorexia nervosa and depressive episode in the course of an inpatient treatment. In addition, there is a lack of studies comparing the tolerability and efficacy of different antidepressants given to anorectic patients of this particular age group. This study compares paroxetine, a specific SRI, with clomipramine, a TCA with SRI activity, concerning the frequency and quality of adverse side effects, the frequency and the reasons for discontinuating the antidepressive treatment and different outcome measurements. METHODS: 83 female patients, aged 10.9 to 18.1 years, who underwent an inpatient treatment at the Departement of Child and Adolescent Psychiatry and Psychotherapy at the University of Wuerzburg, Germany, were enrolled in this retrospective study. All of them met the ICD-10 criteria for anorexia nervosa and depressive episode and received an antidepressant medication with clomipramine or paroxetine. We collected data from basic documentation, treatment reports, and the multiaxial classification (MAS). Outcome measurements were the duration of treatment (days) and the increase of body weight (kg/m2).

  **RESULTS:** The discontinuation of the antidepressive treatment due to adverse side effects or a lack of efficacy was significantly more frequent with clomipramine than paroxetine (33.3 vs. 15.4%). The increase of body weight (2.8 vs. 2.6 kg/m2) was similar in both groups, but the duration of treatment was significantly shorter under paroxetine (71.9 vs. 96.5 days).

  **Conclusions:** A shorter duration of treatment, faster increase of body weight, lower percentage of discontinuating the antidepressive medication and last but not least economic reasons lead to the conclusion, that paroxetine should be preferred in female adolescents with anorexia nervosa and depressive episode. However, prospective studies are needed to confirm our findings.

**Olanzapine & Acute agitation**

- **Intramuscular olanzapine: a review of its use in the management of acute agitation.**

  **Authors:** Wagstaff AJ, Easton J, Scott LJ. - Adis International Limited, Auckland, New Zealand

  **Source:** CNS Drugs. 2005;19(2):147-64. Related Articles, Links

  **Summary:** Intramuscular olanzapine (Zyprexa(R))) is a rapid-acting atypical antipsychotic drug that is also indicated for use in patients with agitation associated with schizophrenia or bipolar mania, the focus of this review. Evidence from three well designed trials indicates that this formulation of olanzapine is at least as effective as intramuscular haloperidol or lorazepam in the treatment of patients with acute agitation associated with schizophrenia or bipolar mania, and has a faster onset of action. Although transient reductions in blood pressure and heart rate may occur in some patients administered intramuscular olanzapine, preliminary evidence of a general lack of clinical effect on the corrected QT (QTc) interval and a low incidence of extrapyramidal symptoms (EPS) is promising. The parenteral formulation of olanzapine appears to offer an effective, fast-acting and generally well tolerated alternative in the treatment of this significant behavioural problem.

**Carbamazepine, Perospirone & Akathisia**

- **Efficacy of carbamazepine against neuroleptic-induced akathisia in treatment with perospirone: case series.**

  **Authors:** Masui T, Kusumi I, Takahashi Y, Koyama T. - Department of Psychiatry, Hokkaido University Graduate School of Medicine, Kita 15 Nishi 7, Kita-ku, Sapporo, Hokkaido 060-8638, Japan.

  **Source:** Prog Neuropsychopharmacol Biol Psychiatry. 2005 Feb;29(2):343-6. Epub 2005 Jan 06. Related Articles, Links

  **Summary:** Neuroleptic-induced akathisia is a distressing side effect of antipsychotics, and it is unmanageable in some cases.
The authors report three cases of schizophrenia whose neuroleptic-induced akathisia did not respond to representative anti-akathisia drugs such as beta-adrenergic antagonists, anticholinergic agents, benzodiazepines and antithistinegerics, and they showed a marked improvement of it without worsening of psychotic symptoms during a combination treatment with carbamazepine and perospirone, a serotonin-dopamine antagonist developed in Japan. As the mechanism of current observation, we assumed that carbamazepine affected the pharmacokinetics of perospirone, and change in the proportion observation, we assumed that carbamazepine affected the mechanism of the current experience.

Topiramate, Anti-convulsant & Eating disorder

**Topiramate for binge eating disorder.**

**Authors:** De Bernardi C, Ferraris S, D’Innella P, Do F, Torre E. - Department of Psychiatry-University of Eastern Piedmont-Novara, Italy


**Summary:** Topiramate is a new anti-convulsant agent that acts on the voltage-activated sodium channels and on the glutamate and GABA receptors; it is furthermore able to reduce hunger and therefore contributes to loss of weight. The authors report the case of a patient suffering from binge eating disorder, who was unresponsive to several therapeutic plans but was successfully treated with topiramate.

Suicidality

CG & Suicidality

**Suicidality and bereavement: complicated grief as psychiatric disorder presenting greatest risk for suicidality.**

**Authors:** Latham AE, Prigerson HG. - The Department of Epidemiology and Public Health at Yale University School of Medicine in New Haven, CT, USA

**Source:** Suicide Life Threat Behav. 2004 Winter;34(4):350-62. Related Articles, Links

**Summary:** The influence of complicated grief (CG) on suicidality among bereaved adults was examined. The Yale Evaluation of Suicidality scale and the Inventory of Complicated Grief-Revised were administered to 309 bereaved adults in face-to-face interviews conducted at baseline (6.2 months post-loss) and at follow-up (10.8 months post-loss). Cross-sectionally, CG was associated with a 6.58 (95% CI: 1.74-18.0) times greater likelihood of “high suicidality” at baseline, and an 11.30 (95% CI: 3.33-38.10) times greater risk of high suicidality at follow-up, after controlling for gender, race, major depressive disorder (MDD), posttraumatic stress disorder (PTSD), and social support. Longitudinally, CG at baseline was associated with an 8.21 (95% CI: 2.49-27.0) times greater likelihood of high suicidality at follow-up, controlling for the above confounders. The study results indicate that CG substantially heightened the risk of suicidality after controlling for important confounders such as MDD and PTSD, suggesting that CG poses an independent psychiatric risk for suicidal thoughts and actions.

Suicidal patients & Affective states

**Desperation & other affective states in suicidal patients.**

**Authors:** Hendin H, Maltsberger JT, Haas AP, Szanto K. - Department of Psychiatry, Columbia University, and the Department of Psychiatry, Center for the Study and Prevention of Suicide and Laboratory of Personality and Development, NY 14642, USA. Kenneth_Conner@urmc.rochester.edu

**Source:** Suicide Life Threat Behav. 2004 Winter;34(4):386-94. Related Articles, Links

**Summary:** Data collected from 26 therapists who were treating patients when they died by suicide were used to identify intense affective states in such patients preceding the suicide. Eleven therapists provided comparable data on 26 patients they had treated who were seriously depressed but not suicidal. Although the two groups had similar numbers diagnosed with MDD, the suicide patients showed a significantly higher total number of intense affects in addition to depression. The acute affect state most associated with a suicide crisis was desperation. Hopelessness, rage, abandonment, self-hatred, and anxiety were also significantly more frequently evidenced in the suicide patients.

Irritability, Impulsivity & Suicidal ideation

**The association of irritability & impulsivity with suicidal ideation among 15- to 20-year-old males.**

**Authors:** Conner KR, Meldrum S, Wiczekorek WF, Duberstein PR, Welte JW. - University of Rochester Medical Center, Department of Psychiatry, Center for the Study and Prevention of Suicide and Laboratory of Personality and Development, NY 14642, USA. Kenneth_Conner@urmc.rochester.edu

**Source:** Suicide Life Threat Behav. 2004 Winter;34(4):363-73. Related Articles, Links

**Summary:** Information on the association of impulsivity and measures of aggression with suicidal ideation in adolescents and young adults is limited. Data were gathered from a community sample of 625 adolescent and young adult males. Analyses were based on multivariate generalized estimating equations. Impulsivity and irritability were associated strongly with suicidal ideation after accounting for alcohol dependence and other aggression-related constructs including psychopathy. Given that irritable, impulsive adolescent males appear to contemplate suicidal behavior, their heightened suicide risk may be anticipated and mitigated.
### Others psychotic disorders

**Disruptive behavior disorders & Risperidone**

- **Short- and long-term efficacy and safety of risperidone in adults with disruptive behavior disorders.**

  **Authors:** Gagiano C, Read S, Thorpe L, Erdeakens M, Van Hove I. - Westdene Research Center, PO Box 29788, Danhof, 9310, South Africa. cctrus@intekom.co.za

  **Source:** Psychopharmacology (Berl). 2005 Jan 25; [Epub ahead of print] Related Articles, Links

  **Summary:** Function in society can be severely affected by disruptive behaviors in adults. OBJECTIVES: To examine the efficacy and safety of risperidone in the treatment of disruptive behavior disorders in intellectually disabled adults. METHODS: Intellectually disabled patients with disruptive behavior disorder were randomly assigned to receive risperidone (n=39) in a flexible dosage ranging from 1 to 4 mg/day (mean dosage, 1.45+/-0.08 mg/day) or placebo (n=36) for 4 weeks of double-blind treatment. Efficacy at endpoint was measured primarily by using the Aberrant Behavior Checklist (ABC); secondary efficacy measures included the Behavior Problems Inventory and Clinical Global Impressions scales. After this 4-week period, patients could enter open-label treatment with risperidone for 48 weeks. RESULTS: Risperidone was well tolerated, and patients treated with risperidone demonstrated significantly greater improvement at endpoint on the ABC than those who received placebo [-27.3 points (52.8% improvement); P=0.036] and also improved on the Behavior Problems Inventory and Clinical Global Impressions ratings. Over the 48-week, open-label follow-up period, there was a further decrease of 6.3 points (P<0.05) on the ABC for patients who initially received risperidone and a decrease of 11.3 points (P<0.05) for patients who initially received placebo and were switched to open-label risperidone. These results were achieved with a mean modal dosage of 1.8 mg/day. Conclusion. Risperidone is efficacious and well tolerated in managing disruptive behavior disorders in adults with intellectual disability.

**MOH & CMLS**

- **Medication-overuse headache: similarities with drug addiction.**

  **Authors:** Calabresi P, Cupini LM. - Clinica Neurologica, Dipartimento di Neuroscienze, Universita Tor Vergata, Rome, Italy & IRCCS Fondazione Santa Lucia, Rome, Italy


  **Summary:** Medication-overuse headache (MOH) is a clinically important entity and it is now well documented that the regular use of acute symptomatic medication by people with migraine or tension-type headache increases the risk of aggravation of the primary headache. MOH is one of the most common causes of chronic migraine-like syndrome. In this article, we analyse the possible mechanisms that underlie sensitization in MOH by comparing these mechanisms with those reported for other forms of drug addiction. Moreover, the evidence for cognitive impulsivity in drug overuse in headache and in other forms of addiction associated with dysfunction of the frontostriatal system will be discussed. An integrative hypothesis for compulsive reward-seeking in MOH will be presented.

**TD symptoms & TDS - PR**

- **Further psychometric properties of the Tourette’s Disorder Scale-Parent Rated version (TODS-PR).**

  **Authors:** Storch EA, Murphy TK, Geffken GR, Soto O, Sajid M, Allen P, Roberti JW, Killiany EM, Goodman WK. - Department of Psychiatry, University of Florida, Box 100234, Gainesville, FL 32610, USA. estorch@psychiatry.ufl.edu

  **Source:** Child Psychiatry Hum Dev. 2004 Winter;35(2):107-20. Related Articles, Links

  **Summary:** This study evaluated the psychometric properties of the Tourette’s Disorder Scale-Parent Rated (TODS-PR), a 15-item parent-rated instrument that assesses a range of common symptoms seen in childhood Tourette’s Disorder (TD) patients including tics, obsessions, compulsions, inattention, and Tourette’s Disorder symptoms. The study found the TODS-PR to be reliable and valid for use in the assessment of TD in children and adolescents.
Prenatal androgens, Sexual orientation & Spatial abilities

- Testing the prenatal androgen hypothesis: measuring digit ratios, sexual orientation, and spatial abilities in adults.

Authors: Van Anders SM, Hampson E. - Department of Psychology, University of Western Ontario, London, ON, Canada


Summary: The present study examined whether the following variables putatively associated with prenatal androgens are inter-related in women: spatial abilities, sexual orientation, and 2nd to 4th finger (digit) length ratio (2D:4D). Participants were 99 healthy premenopausal women tested in the menstrual phase of the ovarian cycle between 0800 and 0930 hr. Women completed the Kinsey scales of sexual orientation, and were either strictly heterosexual (HS; N=79) or not-strictly heterosexual (NHS; N=20). Photocopies of the two hands were collected, and participants completed the revised Vandenberg Mental Rotations test, the Paper Folding test, and a short version of the Guilford-Zimmerman Spatial Orientation Test. Results showed that NHS women exhibited superior spatial ability relative to HS women. No significant difference was found between the HS and NHS women in the 2D:4D digit ratio. There was no association between the digit ratio and spatial performance. These results support an association between increased spatial abilities and heteroflexible sexual orientation, which may possibly be mediated by high prenatal androgens.

Forgiveness, Pain, Anger & Psychological distress —

- Forgive and chronic low back pain: A preliminary study examining the relationship of forgiveness to pain, anger, & psychological distress

Authors: Carson JW, Keefe FJ, Goli V, Fras AM, Lynch TR, Thorp SR, Buechler JL. - Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, North Carolina

Source: J Pain. 2005 Feb;6(2):84-91. Related Articles, Links

Summary: Clinical observations suggest that many patients with chronic pain have difficulty forgiving persons they perceive as having unjustly offended them in some way. By using a sample of 61 patients with chronic low back pain, this study sought to determine the reliability and variability of forgiveness assessments in patients and to examine the relationship of forgiveness to pain, anger, and psychological distress. Standardized measures were used to assess patients’ current levels of forgiveness, forgiveness self-efficacy, pain, anger, and psychological distress. Results showed that forgiveness-related constructs can be reliably assessed in patients with persistent pain, and that patients vary considerably along dimensions of forgiveness. Furthermore, correlational analyses showed that patients who had higher scores on forgiveness-related variables reported lower levels of pain, anger, and psychological distress. Additional analyses indicated that state anger largely mediated the association between forgiveness and psychological distress, as well as some of the associations between forgiveness and pain. These findings indicate that forgiveness can be reliably assessed in patients with persistent pain, and that a relationship appears to exist between forgiveness and important aspects of living with persistent pain. Perspective: This preliminary study suggests there is a relationship between forgiveness and pain, anger, and psychological distress in patients with chronic low back pain. Patients who report an inability to forgive others might be experiencing higher pain and psychological distress that are mediated by relatively higher levels of state anger.

PG & Functional brain

- Decision-making impairments in patients with pathological gambling.

Authors: Braa M, Kalbe E, Labuidda K, Fujwara E, Kessler J, Markowitz HJ. - Department of Physiological Psychology, University of Bielefeld, P.O. Box 100131, 33501 Bielefeld, Germany.


Summary: Pathological gambling (PG) is most likely associated with functional brain changes as well as neuropsychological and personality alterations. Recent research with the Iowa Gambling Task suggests decision-making impairments in PG. These deficits are usually attributed to disturbances in feedback processing and associated functional alterations of the orbitofrontal cortex. However, previous studies with other clinical populations found relations between executive (dorsolateral prefrontal) functions and decision-making using a task with explicit rules for gains and losses, the Game of Dice Task. In the present study, we assessed 25 male PG patients and 25 male healthy controls with the Game of Dice Task. PG patients showed pronounced deficits in the Game of Dice Task, and the frequency of risky decisions was correlated with executive functions and feedback processing. Therefore, risky decisions of PG patients might be influenced by both dorsolateral prefrontal and orbitofrontal cortex dysfunctions.

RLS & Primary care

- Diagnosing restless legs syndrome (RLS) in primary care.


Summary: This paper represents a review of current opinion and information on the effective diagnosis of restless legs syndrome (RLS) in a primary care setting. RLS can be a distressing condition—it can cause serious sleep disturbance and has a significant impact on quality of life comparable to that of depression or type 2 diabetes. The prevalence of adults whose RLS is severe enough to warrant medical advice has been estimated to be approximately 3%, but only a small proportion of these patients currently report having been diagnosed in primary care, despite stating that they have presented to their GP. The
benefits of increased understanding of the symptoms of RLS and how patients present in primary care are discussed, with emphasis on how this will help GPs more effectively diagnose and manage the patients affected. Guidelines on how to diagnose RLS in a primary care setting are given—when a patient presents with sleep disturbance, RLS should be routinely considered and, where existing, be readily diagnosed in a primary care setting on the basis of the patient’s clinical history, a physical examination and with the aid of four questions based on the International RLS Study Group (IRLSSG) four essential diagnostic criteria.

CFS, JRA & Emotional disorders

- Family health and characteristics in chronic fatigue syndrome, juvenile rheumatoid arthritis, and emotional disorders of childhood.

Authors: Rangel L, Garralda ME, Jeffs J, Rose G. - Drs. Rangel and Garralda are with the Academic Unit of Child and Adolescent Psychiatry, Imperial College, London; Mr. Jeffs was with the Metabolic Medicine Unit, Imperial College, London; Dr. Rose is with Collingham Gardens Child Unit, London


Summary: OBJECTIVE: To compare family health and characteristics in children with chronic fatigue syndrome (CFS), in juvenile rheumatoid arthritis (JRA), and emotional disorders. METHOD: Parents of 28 children and adolescents aged 11 to 18 years with CFS, 30 with JRA, and 27 with emotional disorders (i.e., anxiety and/or depressive disorders) were recruited from specialty clinical settings and completed interviews and questionnaires assessing family health problems, parental mental distress, illness attitudes, and family burden of illness. RESULTS: Parents of children with CFS were significantly more likely than those of children with JRA to report a history of CFS-like illness, high levels of mental distress, and a tendency to experience functional impairment in response to physical symptoms. Families of children with CFS were characterized by significantly greater emotional involvement and reported greater family burden related to the child’s illness in comparison with families of children with JRA. Conclusions: CFS in childhood and adolescence is associated with higher levels of parental CFS-like illness, mental distress, emotional involvement, and family illness burden than those observed in association with JRA, a chronic pediatric physical illness.

Chronic headache & Frontal dysfunction

- Frontal lobe dysfunction in patients with chronic migraine: a clinical-neuropsychological study.

Authors: Mongini F, Keller R, Deregbisus A, Barbalonga E, Mongini T. - Department of Clinical Pathophysiology, Headache and Facial Pain Unit, University of Turin, 14 Corso Dogliotti, I-10126 Torino, Italy


Summary: Neuropsychological tests have demonstrated a frontal lobe dysfunction in several psychiatric and neurological disorders. Our purpose was to examine whether similar functional differences would be found in patients with chronic migraine. The Gambling Task (GT), the Tower of Hanoi-3 (TOH-3) and the Object Alternation Test (OAT) were administered to 23 female patients previously treated for chronic migraine and to 23 healthy women who were similar to the patients in age and educational level, and the mean test scores of the two groups were compared (Student’s t and Pearson correlation coefficient). The patient group scored significantly higher than the controls on the TOH-3 and, especially, the OAT. In the patients, no significant relationship was found between the neuropsychological test scores and those for the Minnesota Multiple Personality Inventory (MMPI), the Spielberg State-Trait Anxiety Inventory (STAI), and the Beck Depression Inventory (BDI). In conclusion, the data suggest a relation between chronic headache and dorsolateral function (as tested by the TOH-3) and orbitofrontal function (as tested by the OAT). The decision-making function related to ventromedial prefrontal cortex (tested by the GT) did not show a statistically significant difference between patients and controls. These neuropsychological findings seem to be partly independent of the patient’s psychological traits and psychiatric disorders.

Eating disorders

Androgen Antagonist, Citalopram & Bulimia Nervosa

- Effects of the Androgen Antagonist Flutamide and the Serotonin Reuptake Inhibitor Citalopram in Bulimia Nervosa: A Placebo-Controlled Pilot Study.

Authors: Sundblad C, Landen M, Eriksson T, Bergman L, Eriksson E. - Departments of Pharmacology and Clinical Neuroscience, Göteborg University, Göteborg; double daggers: Department of General and Forensic Psychiatry, Lund University, Malmo University Hospital, Malmo and section signPrivate Unit for Child Psychiatry, Göteborg, Sweden


Summary: Prompted by previous studies suggesting that bulimia nervosa in women may be associated with elevated serum levels of testosterone, we have evaluated the possible effect of androgen antagonism in this condition. To this end, women meeting the DSM-IV criteria of bulimia nervosa, purging type, were treated in a one-center study with the androgen receptor antagonist flutamide (n = 9), the serotonin reuptake inhibitor citalopram (n = 15), flutamide plus citalopram (n = 10), or placebo (n = 12) for 3 months using a double-blind design. Self-rated global assessment of symptom intensity suggests all active treatments to be superior to placebo. The reduction in binge eating compared with baseline was statistically significant in both groups given flutamide but not in the groups given citalopram only or placebo. A moderate and reversible increase in serum transaminase levels led to discontinuation in two subjects in the flutamide group. It is concluded that blockade of androgen receptors may reduce some of the symptoms of bulimia nervosa in women.

CBD Fluoxetine & BED


Authors: Grilo CM, Masheb RM, Wilson GT. - Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut.
**Source:** Biol Psychiatry. 2005 Feb 1;57(3):301-9. Related Articles, Links

**Summary:** BACKGROUND: Cognitive behavioral therapy (CBT) and certain medications have been shown to be effective for binge eating disorder (BED), but no controlled studies have compared psychological and pharmacological therapies. We conducted a randomized, placebo-controlled study to test the efficacy of CBT and fluoxetine alone and in combination for BED. METHODS: 108 patients were randomized to one of four 16-week individual treatments: fluoxetine (60 mg/day), placebo, CBT plus fluoxetine (60 mg/day) or CBT plus placebo. Medications were provided in double-blind fashion. RESULTS: Of the 108 patients, 86 (80%) completed treatments. Remission rates (zero binges for 28 days) for completers were: 29% (fluoxetine), 30% (placebo), 55% (CBT+fluoxetine), and 73% (CBT+placebo). Intent-to-treat (ITT) remission rates were: 22% (fluoxetine), 26% (placebo), 50% (CBT+fluoxetine), and 61% (CBT+placebo). Completer and ITT analyses on remission and dimensional measures of binge eating, cognitive features, and psychological distress produced consistent findings. Fluoxetine was not superior to placebo, CBT+fluoxetine and CBT+placebo did not differ, and both CBT conditions were superior to fluoxetine and to placebo. Weight loss was modest, did not differ across treatments, but was associated with binge eating remission. Conclusions: CBT, but not fluoxetine, demonstrated efficacy for the behavioral and psychological features of BED, but not obesity.

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**ARABPSYNET CONDEMNS LONDON AND SHARM EL SHEIKH BOMBINGS**

Arabpsynet web portal for Mental Health condemns the atrocious Inhumanity of those who planted the bombs that shocked London on 7 and 21 July 2005 and killed approximately 54 victims and injured nearly 700 as well as the terrorist attacks on Sharm El Sheikh which killed nearly 70; and injured nearly 120.Arabpsyne also condemns the inhumanity of the killers of Ehab El Sherif, head of Egypt’s diplomatic mission in Iraq. The crimes in those situations reflect humanity in short supply. The trouble is that these crimes are committed in the name of Islam.

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**XIII™ World Congress of Psychiatry, Cairo, September 10-15, 2005**

**WIAMH SYMPOSIUM**

**Sponsor:** World Islamic Association for Mental Health: WIAMH

**Title:** Recent Developments in Culturally Appropriate Mental Health Care Among Muslims

**Topic:** 04 Social and Cultural Psychiatry

**Language of the presentation:** ENGLISH

**Presenters /Authors:**

**Abstract:** Psychiatry is a Western import to the Muslims, pioneer Muslim psychiatrists felt that for psychiatry to work more effectively in the Muslim World, all aspect of the psychiatric process, have to be adapted to the Islamic cultural context. The World Islamic Association for Mental Health (WIAMH) founded two decades ago to promote these efforts is sponsoring this symposium. In this workshop, a number of world renowned mental health workers will participate and present the progress they have developed utilizing the Islamic principles. Professor Dr. El-Sherbeeny will discuss “Overview of Psychiatry in Arab Culture”. Dr Wahida Valiante will present a paper entitled “Towards Development of an Islamic Approach to Family Therapy”. Dr El Rady and Dr Prof. Osama Tawakol will discuss: “The Influence of Culture and Religion on Mental Health Treatment: A Stigma Revisited”. Dr Farouk El Sendiony will present a paper entitled: “The Cultural Differences in the Manifestation of Torture”. Dr Elizabeth Coker will discuss: “Religion, Morality, and Psychiatric Stigma in Egypt: Implications for the development of culturally appropriate mental health care and education”. The format of the workshop will encourage a discussion between the panel members and the audience and we hope to generate a number of valuable recommendations.

**Additional Information:**

- The ability to diagnose, and treat psychiatric disorders is enhanced when clinicians fully integrate an appreciation of the cultural context of patients. It’s felt that this integration of the Muslim cultural context into the diagnostic and treatment plan will make modern psychiatry—which is a recent western import to the Muslim World—work more effectively.

**Articles:**


These observations have led a number of mental health workers around the Muslim World to develop innovative methods for the promotion of mental health and the prevention of mental illness.

**Arabpsynet e.Journal:** Nº 6 – April – May – June 2005

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