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# کراچی نفسیاتی ہسپتال، کراچی منشیات ہسپتال

زیر اشراف  
ڈاکٹر سید مبین اختر  
(اسنڈ یافتہ امریکہ)

برائے امراض ذہنی، جنسی، روحانی و منشیات  
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# KARACHI PSYCHIATRIC HOSPITAL

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محمد رفیق

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## DOSE-DEPENDENT RISK OF MALFORMATIONS WITH ANTIEPILEPTIC DRUGS: AN ANALYSIS OF DATA FROM THE EURAP EPILEPSY AND PREGNANCY REGISTRY

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Dr, Prof Torbjörn Tomson MD & Colleagues - The Lancet Neurology, July 2011

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### SUMMARY

#### Background

Prenatal exposure to antiepileptic drugs is associated with a greater risk of major congenital malformations, but there is inadequate information on the comparative teratogenicity of individual antiepileptic drugs and the association with dose. We aimed to establish the risks of major congenital malformations after monotherapy exposure to four major antiepileptic drugs at different doses.

#### Methods

The EURAP epilepsy and pregnancy registry is an observational cohort study representing a collaboration of physicians from 42 countries. We prospectively monitored pregnancies exposed to monotherapy with different doses of four common drugs: carbamazepine, lamotrigine, valproic acid, or phenobarbital. Our primary endpoint was the rate of major congenital malformations detected up to 12 months after birth. We assessed pregnancy outcomes according to dose at the time of conception irrespective of subsequent dose changes.

#### Findings

After excluding pregnancies that ended in spontaneous abortions or chromosomal or genetic abnormalities, those in which the women had treatment changes in the first trimester, and those involving other diseases

or treatments that could affect fetal outcome, we assessed rates of major congenital malformations in 1402 pregnancies exposed to carbamazepine, 1280 on lamotrigine, 1010 on valproic acid, and 217 on phenobarbital. An increase in malformation rates with increasing dose at the time of conception was recorded for all drugs. Multivariable analysis including ten covariates in addition to treatment with antiepileptic drugs showed that the risk of malformations was greater with a parental history of major congenital malformations (odds ratio 4.4, 95% CI 2.06-9.23). We noted the lowest rates of malformation with less than 300 mg per day lamotrigine (2.0% [17 events], 95% CI 1.19-3.24) and less than 400 mg per day carbamazepine (3.4% [5 events], 95% CI 1.11-7.71). Compared with lamotrigine monotherapy at doses less than 300 mg per day, risks of malformation were significantly higher with valproic acid and phenobarbital at all investigated doses, and with carbamazepine at doses greater than 400 mg per day.

#### Interpretation

The risk of major congenital malformations is influenced not only by type of antiepileptic drug, but also by dose and other variables, which should be taken into account in the management of epilepsy in women of childbearing potential.

## FUNCTIONAL IMPAIRMENT IN ELDERLY PATIENTS WITH MILD COGNITIVE IMPAIRMENT AND MILD ALZHEIMER DISEASE

Patrick J. Brown, PhD & Colleagues - Arch Gen Psychiatry. 2011

**Context** The original mild cognitive impairment (MCI) criteria exclude substantial functional deficits, but recent reports suggest otherwise. Identifying the extent, severity, type, and correlates of functional deficits that occur in MCI and mild Alzheimer disease (AD) can aid in early detection of incipient dementia and can identify potential mechanistic pathways to disrupted instrumental activities of daily living (IADLs).

**Objectives** To examine the number, type, and severity of functional impairments and to identify the clinical characteristics associated with functional impairment across patients with amnesic MCI (aMCI) and those with mild AD.

**Design** Study using baseline data from the Alzheimer's Disease Neuroimaging Initiative.

**Setting** Multiple research sites in the United States and Canada.

**Patients** Samples included 229 control individuals, 394 patients with aMCI, and 193 patients with AD.

**Main Outcome Measure** The 10-item Pfeffer Functional Activities Questionnaire (FAQ) assessed function.

**Results** Informant-reported FAQ deficits were common in patients with aMCI (72.3%) and AD (97.4%) but were rarely self-reported by controls (7.9%). The average severity per FAQ deficit did not differ between patients with aMCI and controls; both were less impaired than patients with AD ( $P < .001$ ). Two FAQ items (remembering appointments,

family occasions, holidays, and medications and assembling tax records, business affairs, or other papers) were specific (specificity estimate, 0.95) in differentiating the control group from the combined aMCI and AD groups (only 34.0% of patients with aMCI and 3.6% of patients with AD had no difficulty with these 2 items). The severity of FAQ deficits in the combined aMCI and AD group was associated with worse Trail Making Test, part A scores and smaller hippocampal volumes ( $P < .001$  for both). Within the aMCI group, functionally intact individuals had greater hippocampal volumes and better Auditory Verbal Learning Test 30-minute delay and Trail Making Test, part A ( $P < .001$  for each) scores compared with individuals with moderate or severe FAQ deficits. Patients with a high number of deficits were more likely to express the apolipoprotein 4 allele (63.8%) compared with patients with no (46.8%) or few (48.4%) functional deficits.

**Conclusions** Mild IADL deficits are common in individuals with aMCI and should be incorporated into MCI criteria. Two IADLs—remembering appointments, family occasions, holidays, and medications and assembling tax records, business affairs, or other papers—appear to be characteristic of clinically significant cognitive impairment. In patients with aMCI, impairment in memory and processing speed and greater medial temporal atrophy were associated with greater IADL deficits.



# DISENTANGLING STRUCTURAL BRAIN ALTERATIONS ASSOCIATED WITH VIOLENT BEHAVIOR FROM THOSE ASSOCIATED WITH SUBSTANCE USE DISORDERS

BORIS SCHIFFER, PHD & Colleagues - Arch Gen Psychiatry June 6, 2011

**Context** Studies aimed at identifying structural brain alterations associated with persistent violent behavior or psychopathy have not adequately accounted for a lifetime history of substance misuse. Thus, alterations in gray matter (GM) volume that have been reported to be correlates of violent behavior and/or psychopathy may instead be related to lifelong substance use disorders (SUDs).

**Objective** To identify alterations in GM volume associated with violent behavior and those associated with lifelong SUDs.

**Design** Cross-sectional study.

**Setting** Participants were recruited from penitentiaries, forensic hospitals, psychiatric outpatient services, and communities in Germany. Structural magnetic resonance imaging was performed at a university hospital.

**Participants** Four groups of men were compared: 12 men with SUDs who exhibited violent behavior (hereafter referred to as violent offenders), 12 violent offenders without SUDs, 13 men with SUDs who did not exhibit violent behavior (hereafter referred to as nonoffenders), and 14 nonoffenders without SUDs.

**Main Outcome Measures** Voxel-based morphometry was used to analyze high-resolution magnetic resonance imaging scans. Assessments of mental disorders,

psychopathy (using the Psychopathy Checklist-Screening Version), aggressive behavior, and impulsivity were conducted by trained clinicians.

**Results** Compared with nonoffenders, violent offenders presented with a larger GM volume in the amygdala bilaterally, the left nucleus accumbens, and the right caudate head and with less GM volume in the left insula. Men with SUDs exhibited a smaller GM volume in the orbitofrontal cortex, ventromedial prefrontal cortex, and premotor cortex than did men without SUDs. Regression analyses indicated that the alterations in GM volume that distinguished the violent offenders from nonoffenders were associated with psychopathy scores and scores for lifelong aggressive behavior. The GM volumes of the orbitofrontal cortex and prefrontal cortex that distinguished the men with SUDs from the men without SUDs were correlated with scores for response inhibition.

**Conclusions** These findings suggest that a greater GM volume in the mesolimbic reward system may be associated with violent behavior and that reduced GM volumes in the prefrontal cortex, orbitofrontal cortex, and premotor area characterize men with SUDs.

<http://archpsyc.ama-assn.org/cgi/content/abstract/archgenpsychiatry.2011.61v2?>

## COLLABORATIVE DEPRESSION CARE MANAGEMENT AND DISPARITIES IN DEPRESSION TREATMENT AND OUTCOMES

Yuhua Bao, PhD & Colleagues - Arch Gen Psychiatry. 2011

**Context** Collaborative depression care management (DCM), by addressing barriers disproportionately affecting patients of racial/ethnic minority and low education, may reduce disparities in depression treatment and outcomes.

**Objective** To examine the effects of DCM on treatment disparities by education and race/ethnicity in older depressed primary care patients.

**Design** Analysis of data from the randomized controlled trial Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT).

**Setting** Twenty primary care practices.

**Participants** A total of 396 individuals 60 years or older with major depression. We conducted model-based analysis to estimate potentially differential intervention effects by education, independent of those by race/ethnicity (and vice versa).

**Intervention** Algorithm-based recommendations to physicians and care management by care managers.

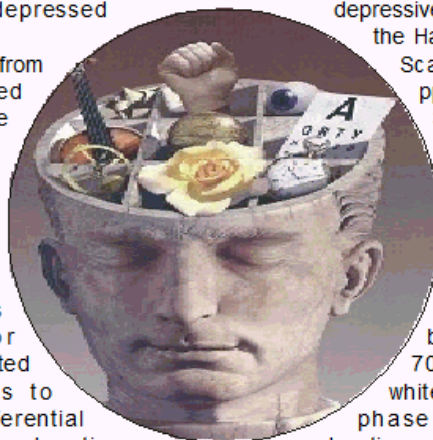
**Main Outcome Measures** Antidepressant use, depressive symptoms, and intensity of DCM over 2 years.

**Results** The PROSPECT intervention had a larger and more lasting effect in

less-educated patients. At month 12, the intervention increased the rate of adequate antidepressant use by 14.2 percentage points (pps) (95% confidence interval [CI], 1.7 to 26.4 pps) in the no-college group compared with a null effect in the college-educated group (-9.2 pps [95% CI, -25.0 to 2.7 pps]); at month 24, the intervention reduced depressive symptoms by 2.6 pps on the Hamilton Depression Rating Scale (95% CI, -4.6 to -0.4 pps) in no-college patients, 3.8 pps (95% CI, -6.8 to -0.4) more than in the college group. The intervention benefitted non-Hispanic white patients more than minority patients. Intensity of DCM received by minorities was 60% to 70% of that received by white patients after the initial phase but did not differ by education.

**Conclusions** The PROSPECT intervention substantially reduced disparities by patient education but did not mitigate racial/ethnic disparities in depression treatment and outcomes. Incorporation of culturally tailored strategies in DCM models may be needed to extend their benefits to minorities.

<http://archpsyc.ama-assn.org/cgi/content/abstract/68/6/627>



## DECLINING AUTOPSY RATES AND SUICIDE MISCLASSIFICATION

**Nestor D. Kapusta, MD & Colleagues**  
*Arch Gen Psychiatry June 6, 2011*

**Context** Suicides are prone to misclassification during death ascertainment procedures. This problem has generated frequent criticism of the validity of suicide mortality statistics.

**Objective** To employ an external measure of the validity of cause-of-death statistics (ie, national autopsy rates) and to examine potential misclassification of suicide across countries from Europe to Central and Northern Asia.

**Design** Cross-national analysis.

**Setting** Thirty-five countries.

**Participants** Aggregated mortality data.

**Main Outcome Measures** Data from 35 countries during the period from 1979 to 2007 were used to analyze the association of suicide rates with autopsy rates and death rates of undetermined and ill-defined causes, respectively. Analyses were cross-sectional and longitudinal.

**Results** Cross-sectionally, a 1% difference in autopsy rates among nations was associated with a suicide rate difference of 0.49 per 100 000 population. Longitudinally, a 1% decrease in the autopsy rate aligned with a decrease of 0.42 per 100 000 population in the suicide rate. These cross-sectional and longitudinal associations were robust after adjustment for unemployment, degree of urbanization, and prevalence of undetermined or ill-defined deaths. Associations strengthened when analyses were confined to 19 European Union member countries.

**Conclusion** Autopsy rates may spatially and temporally affect the validity of suicide mortality statistics. Caution should be exercised in comparing international suicide rates and evaluating interventions that target suicide rate reduction.

<http://archpsyc.ama-assn.org/cgi/content/abstract/archgenpsychiatry.2011.66v1?>

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## SYSTEMATIC REVIEW OF EARLY CARDIOMETABOLIC OUTCOMES OF THE FIRST TREATED EPISODE OF PSYCHOSIS

Debra L. Foley, PhD; Katherine I. Morley, PhD - Arch Gen Psychiatry. 2011

**Context** The increased mortality associated with schizophrenia is largely due to cardiovascular disease. Treatment with antipsychotics is associated with weight gain and changes in other cardiovascular risk factors. Early identification of modifiable cardiovascular risk factors is a clinical imperative but prospective longitudinal studies of the early cardiometabolic adverse effects of antipsychotic drug treatment other than weight gain have not been previously reviewed.

**Objectives** To assess the methods and reporting of cardiometabolic outcome studies of the first treated episode of psychosis, review key findings, and suggest directions for future research.

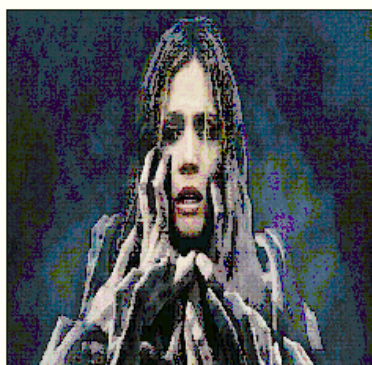
**Data Sources** PsycINFO, MEDLINE, and Scopus from January 1990 to June 2010.

**Study Selection** Subjects were experiencing their first treated episode of psychosis. Subjects were antipsychotic naive or had been exposed to antipsychotics for a short known period at the beginning of the study. Cardiometabolic indices were assessed. Studies used a longitudinal design.

**Data Extraction** Sixty-four articles were identified describing 53 independent studies; 25 studies met inclusion criteria and were retained for detailed review.

**Data Synthesis** Consolidated Standards of Reporting Trials and Strengthening the Reporting of Observational Studies in Epidemiology checklists were used to assess the methods and reporting of studies. A qualitative review of findings was conducted.

**Conclusions** Two key hypotheses were identified based on this review: (1) in general, there is no difference in cardiovascular risk assessed by weight or metabolic indices between individuals with an untreated first episode of psychosis and healthy controls and (2) cardiovascular risk increases after first exposure to any antipsychotic drug. A rank



order of drugs can be derived but there is no evidence of significant class differences. Recommended directions for future research include assessing the effect on cardiometabolic outcomes of medication adherence and dosage effects, determining the therapeutic window for antipsychotic use in adults and youth, and testing for moderation of outcomes by demographic factors, including sex and age, and clinical and genetic factors.

[http://archpsyc.ama-assn.org/  
cgi/content/abstract/68/6/609](http://archpsyc.ama-assn.org/cgi/content/abstract/68/6/609)

## AN EFFECTIVENESS TRIAL OF GROUP COGNITIVE BEHAVIORAL THERAPY FOR PATIENTS WITH PERSISTENT DEPRESSIVE SYMPTOMS IN SUBSTANCE ABUSE TREATMENT

Katherine E. Watkins, MD, MSHS & Colleagues - Arch Gen Psychiatry. 2011

**Context** Although depression frequently co-occurs with substance abuse, few individuals entering substance abuse treatment have access to effective depression treatment.

**Objective** The Building Recovery by Improving Goals, Habits, and Thoughts (BRIGHT) study is a community-based effectiveness trial that compared residential substance abuse treatment with residential treatment plus group cognitive behavioral therapy for depression delivered by substance abuse treatment counselors. We hypothesized that intervention clients would have improved depression and substance use outcomes compared with those of clients receiving usual care.

**Design** A nonrandomized controlled trial using a quasi-experimental intent-to-treat design in which 4 sites were assigned to alternate between the intervention and usual care conditions every 4 months for 2 years.

**Setting** Four treatment programs in Los Angeles County.

**Participants** We screened 1262 clients for persistent depressive symptoms (Beck Depression Inventory-II score  $>17$ ). We assigned 299 clients to receive either usual care ( $n = 159$ ) or usual care plus the intervention ( $n = 140$ ). Follow-up rates

at 3 and 6 months after the baseline interview were 88.1% and 86.2%, respectively, for usual care and 85.7% and 85.0%, respectively, for the intervention group.

**Intervention** Sixteen 2-hour group sessions of cognitive behavioral therapy for depression.

**Main Outcome Measures** Change in depression symptoms, mental health functioning, and days of alcohol and problem substance use.

**Results** Intervention clients reported significantly fewer depressive symptoms ( $P < .001$  at 3 and 6 months) and had improved mental health functioning ( $P < .001$  at 3 months and  $P < .01$  at 6 months). At 6 months, intervention clients reported fewer drinking days ( $P < .05$ ) and fewer days of problem substance use ( $P < .05$ ) on days available.

**Conclusions** Providing group cognitive behavioral therapy for depression to clients with persistent depressive symptoms receiving residential substance abuse treatment is associated with improved depression and substance use outcomes. These results provide support for a new model of integrated care.

<http://archpsyc.ama-assn.org/cgi/content/abstract/68/6/577>

## A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL OF OLANZAPINE PLUS SERTRALINE VS OLANZAPINE PLUS PLACEBO FOR PSYCHOTIC DEPRESSION

The Study of Pharmacotherapy of Psychotic Depression (STOP-PD)

Barnett S. Meyers & Colleagues - Arch Gen Psychiatry. 2009

**Context** Evidence for the efficacy of combination pharmacotherapy has been limited and without positive trials in geriatric patients with major depression (MD) with psychotic features.

**Objectives** To compare remission rates of MD with psychotic features in those treated with a combination of atypical antipsychotic medication plus a serotonin reuptake inhibitor with those treated with antipsychotic monotherapy; and to compare response by age.

**Design** Twelve-week, double-blind, randomized, controlled trial.

**Setting** Clinical services of 4 academic sites.

**Patients** Two hundred fifty-nine subjects with MD with psychotic features randomized by age (<60 or ≥60 years) (mean [standard deviation (SD)], 41.3 [10.8] years in 117 younger adults vs 71.7 [7.8] years in 142 geriatric participants).

**Intervention** Target doses of 15 to 20 mg of olanzapine per day plus masked sertraline or placebo at 150 to 200 mg per day.

**Main Outcome Measure** Remission rates of MD with psychotic features.

**Results** Treatment with olanzapine/sertraline was associated with

higher remission rates during the trial than olanzapine/placebo (odds ratio [OR], 1.28; 95% confidence interval [CI], 1.12-1.47;  $P < .001$ ); 41.9% of subjects who underwent combination therapy were in remission at their last assessment compared with 23.9% of subjects treated with monotherapy ( $21 = 9.53$ ,  $P = .002$ ). Combination therapy was comparably superior in both younger (OR, 1.25; 95% CI, 1.05-1.50;  $P = .02$ ) and older (OR, 1.34; 95% CI, 1.09-1.66;  $P = .01$ ) adults. Overall, tolerability was comparable across age groups. Both age groups had significant increases in cholesterol and triglyceride concentrations, but statistically significant increases in glucose occurred only in younger adults. Younger adults gained significantly more weight than older subjects (mean [SD], 6.5 [6.6] kg vs 3.3 [4.9] kg,  $P = .001$ ).

**Conclusions:** Combination pharmacotherapy is efficacious for the treatment of MD with psychotic features. Future research must determine the benefits vs risks of continuing atypical antipsychotic medications beyond 12 weeks.

<http://archpsyc.ama-assn.org/cgi/content/abstract/66/8/838?>



## INTEGRATING NEUROBIOLOGICAL MARKERS OF DEPRESSION

Tim Hahn, PhD & Colleagues - Arch Gen Psychiatry. 2011

**Context** Although psychiatric disorders are, to date, diagnosed on the basis of behavioral symptoms and course of illness, the interest in neurobiological markers of psychiatric disorders has grown substantially in recent years. However, current classification approaches are mainly based on data from a single biomarker, making it difficult to predict disorders characterized by complex patterns of symptoms.

**Objective** To integrate neuroimaging data associated with multiple symptom-related neural processes and demonstrate their utility in the context of depression by deriving a predictive model of brain activation.

**Design** Two groups of participants underwent functional magnetic resonance imaging during 3 tasks probing neural processes relevant to depression.

**Setting** Participants were recruited from the local population by use of advertisements; participants with depression were inpatients from the Department of Psychiatry, Psychosomatics, and Psychotherapy at the University of Wuerzburg, Wuerzburg, Germany.

**Participants** We matched a sample of 30 medicated, unselected patients with depression by age, sex, smoking status, and handedness with 30 healthy volunteers.

**Main Outcome Measure** Accuracy of

single-subject classification based on whole-brain patterns of neural responses from all 3 tasks.

**Results** Integrating data associated with emotional and affective processing substantially increases classification accuracy compared with single classifiers. The predictive model identifies a combination of neural responses to neutral faces, large rewards, and safety cues as nonredundant predictors of depression. Regions of the brain associated with overall classification comprise a complex pattern of areas involved in emotional processing and the analysis of stimulus features.

**Conclusions** Our method of integrating neuroimaging data associated with multiple, symptom-related neural processes can provide a highly accurate algorithm for classification. The integrated biomarker model shows that data associated with both emotional and reward processing are essential for a highly accurate classification of depression. In the future, large-scale studies will need to be conducted to determine the practical applicability of our algorithm as a biomarker-based diagnostic aid.

<http://archpsyc.ama-assn.org/cgi/search?fulltext=integrating+neurobiological+markers+of+depression>

## ACCEPTANCE-BASED BEHAVIORAL THERAPY FOR GAD: EFFECTS ON OUTCOMES FROM THREE THEORETICAL MODELS

Treanor M et al. *Depress Anxiety* 2011 Feb

Acceptance-based behavioral therapy (ABBT), which has shown efficacy for generalized anxiety disorder (GAD) in preliminary trials, targets patients' negative judgments about, and avoidance of, distressing emotions; rigid attempts to control internal experiences; and avoidance of engagement in important life activities. The current researchers examined ABBT's efficacy and effects on elements central to other models of GAD - e.g., emotion dysregulation, intolerance of uncertainty, and perceived lack of control.

The 31 participants with GAD (71% female; 87% white) were randomized to ABBT or a waitlist control condition. Most patients had comorbidities (major depression, 9; social phobia, 5; panic disorder, 4; obsessive-compulsive disorder, 4). Nine subjects were on stable doses of psychotropic medications. ABBT included psychoeducation, mindfulness exercises, and encouragement to re-engage in activities. Active treatment, compared with waitlist, yielded significantly greater decreases in fear of emotions and difficulties in emotion regulation. Tolerance of uncertainty and perception of control increased significantly. These changes correlated with improvements in GAD symptoms and persisted at 3- and 9-month follow-ups.

**Comment:** Several effective cognitive-behavioral therapies now exist for GAD, each based on a distinct theoretical framework regarding the core issue in this disorder. This study confirms that a mindfulness- and acceptance-based treatment is effective, compared with waitlist control. More rigorous studies of ABBT, especially in comparison with other effective treatments, are needed. However, these results show that ABBT

actually addresses and improves symptoms targeted by three other CBT treatments for GAD. These treatments may address all of these factors, or a particular factor may need to be addressed to achieve efficacy. Further studies can identify the most important factor(s) to target, thus increasing both our understanding of GAD and the efficacy of treatment.

<http://psychiatry.jwatch.org/cgi/content/full/2011/328/1>

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## MEMANTINE FOR PATIENTS WITH PARKINSON'S DISEASE DEMENTIA OR DEMENTIA WITH LEWY BODIES: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Emre M et al *Lancet Neurol* 2010 Oct

**Memantine**, an N-methyl D-aspartate (NMDA) receptor antagonist that modulates the neurotransmitter glutamate, is modestly effective for Alzheimer disease dementia. Preliminary studies have suggested that memantine may improve cognition in Lewy body spectrum dementias, including Parkinson disease dementia (PDD) and dementia with Lewy bodies (DLB). In addition, controversy persists regarding the relationship between DLB and PDD. The clinical and pathological features of these disorders overlap substantially. However, PDD and DLB may differ enough to warrant different treatment approaches. Researchers conducted a 24-week, multicenter, manufacturer-funded, randomized clinical trial of memantine (20 mg once daily) in patients with mild-to-moderate PDD (116 patients) or DLB (74 patients). Cognition, behavior, and activities of daily living (ADL) function were assessed by standard measures.

By the study's end, scores on a clinical global impression of change measure and neuropsychiatric symptoms showed a modest but statistically significant improvement with memantine compared with placebo in patients with DLB. For patients with PDD, outcomes of

memantine treatment were no different than those of placebo. ADL function, motor performance, and caregiver burden were unchanged in both groups. Notably, cognitive test scores did not improve with memantine in either disease group. Memantine was comparable to placebo on measures of safety and tolerability.

**Comment:** The conclusions that can be drawn from this study are limited by the very modest effects of treatment and lack of a prespecified primary outcome measure. At best, memantine at 20 mg daily has a small and nonspecific effect in Lewy body spectrum dementias. This study is unlikely to increase prescribing of memantine for PDD and DLB because the modest benefits of treatment do not outweigh the cost and inconvenience of the additional medication. Although the findings suggest a modest effect in DLB and none in PDD, this study does not elucidate the issue of differential treatment response between the two dementia types, as neither group changed sufficiently to identify such differences.



<http://Neurology.jwatch.org/cgi/content/full/2010/1019/4>



## REMEMBER THE FUTURE: WORKING MEMORY TRAINING DECREASES DELAY DISCOUNTING AMONG STIMULANT ADDICTS

Bickel WK et al - Biol Psychiatry Feb 2011

**Ignoring** or discounting delayed future rewards (i.e., "delay discounting") is a central characteristic of risk takers and impulsive people who prefer a smaller immediate reward to a later, more substantial one. This study of 27 patients receiving treatment for stimulant misuse examined whether exercises designed to enhance memory of past events would decrease delay discounting.

All patients underwent a training program for working memory (e.g., forward and reverse digit recall) and were randomized to receive monetary reinforcement based on individual performance (active group) or based on the performance of a member of the active group (control group). Before and after training, the participants were tested on frontal behavior (e.g., disinhibition and executive function), working memory, learning by trial and error, episodic memory, verbal learning and memory, and delay discounting. The last was assessed by giving subjects choices between immediately receiving small amounts of money and receiving larger amounts of money later.

Active training significantly decreased delay discounting rates by 50%. Delay discounting rates increased in the control group by 50% (not statistically significant). In the active group, a larger number of training sessions and higher posttraining working memory scores were associated with greater decreases in delay discounting rates. Training affected no other measures.

**Comment:** Valuing the future seems to be linked to remembering the past. The authors theorize that delay discounting results from an imbalance between an impulsive decision system, which is located in limbic and paralimbic regions and is associated with response to immediate reinforcers, and a frontal executive system that drives planning and deferred reinforcement. Whereas training multiple executive functions has not been helpful for addiction, training the single function of working memory may enhance the ability to compare the value of future and current rewards and may promote more-adaptive decision making.

<http://psychiatry.jwatch.org/cgi/content/full/2011/328/2>

## CHILDREN OF DEPRESSED MOTHERS 1 YEAR AFTER REMISSION OF MATERNAL DEPRESSION: FINDINGS FROM THE STAR\*D-CHILD STUDY

Wickramaratne P et al. Am J Psychiatry 2011 Mar 15

**Are** children helped in the longer term when their depressed mothers respond to treatment? Researchers have now reported 1-year follow-up data on this question in a substudy of the STAR\*D treatment study of major depressive disorder in adults.

Quarterly assessments of the children concentrated on mood, anxiety, and disruptive disorders. Of the 151 eligible dyads, 127 had at least one follow-up (children's mean age, 12 years; 55% male). Of 64 mothers with remission and no later relapse, 36 mothers remitted within 3 months (early group), and 28 mothers remitted between 3 and 12 months (late group); these children were assessed for 1 year after remission. In children of 16 mothers whose disease never remitted, assessments occurred for 2 years.

The early group had the highest household income, the highest proportion of mothers who were married, and the lowest baseline psychopathology in the offspring. The analyses controlled for these significant differences. At follow-up, children of early remitters had significantly better functioning and fewer psychiatric symptoms than children of nonremitters. Conduct disorder symptoms significantly improved from baseline in children of both early and late remitters but worsened in children of nonremitters. Children's diagnoses or psychiatric treatment did not affect these outcomes.

**Comment:** These findings are similar to those in the 3-month follow-up: Early remission and, to a lesser extent, late remission in mothers

are associated with large benefits to children. The results reinforce the need for strategies that address treatment-resistant depression and maternal remission. For example, adult therapists could be available at child psychiatry clinics, and clinicians could educate parents that optimizing their treatment would help their children.

<http://psychiatry.jwatch.org/cgi/content/full/2011/404/2>

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## LONGITUDINAL FOLLOW-UP OF BIPOLAR DISORDER IN WOMEN WITH PREMENSTRUAL EXACERBATION: FINDINGS FROM STEP-BD

Dias RS et al. Am J Psychiatry Feb 2011

**Up** to two thirds of women with affective disorders have reported premenstrual exacerbation of mood, but premenstrual mood worsening has not been detected in small studies of bipolar disorder. Using data on menstruating women with bipolar disorder (age range, 18-40) from the STEP-BD study, investigators examined the potential impact of premenstrual mood exacerbation on illness course. Analyses adjusted for psychotropic medications, hormonal contraceptives, comorbidities, number of mood episodes in the previous year, and irregular menstrual cycles.

Of 293 women, 65% reported premenstrual exacerbation of mood symptoms. At 1-year follow-up, those with self-reported premenstrual exacerbation had more mood episodes (primarily depression) than those without - but not more rapid cycling. The researchers examined time to relapse in a partially overlapping cohort of 129 women who had recovered by study entry; 51% had reported premenstrual exacerbation. When relapse was defined to include subsyndromal episodes, women reporting premenstrual exacerbation had greater

risk for relapse and shorter time to relapse (4.5 months vs. 8.5 months) than those without, but this difference became nonsignificant after adjustment for the greater number of mood episodes reported by those with premenstrual exacerbation.

**Comment:** Taken together, the findings suggest that women with premenstrual cycling are likely to experience more-severe and more-frequent episodes of bipolar disorder, but not more rapid cycling per se. Sensitivity and susceptibility of mood to fluctuating levels of ovarian steroids may be contributory. That less premenstrual exacerbation of mood is seen prospectively than reported retrospectively suggests that some women may incorrectly attribute some perimenstrual mood fluctuations to their bipolar disorder. Clinicians can help patients better distinguish one from the other and can expect a more difficult course for many women with premenstrual exacerbation.

<http://psychiatry.jwatch.org/cgi/content/full/2011/314/1>



# LONG-ACTING RISPERIDONE AND ORAL ANTIPSYCHOTICS IN UNSTABLE SCHIZOPHRENIA

( FOR THE CSP555 RESEARCH GROUP)

Rosenheck RA et al. N Engl J Med Mar 2011

**Poor** adherence to antipsychotic medications is thought to frequently cause poor outcomes in schizophrenia. Whether use of injectable depot antipsychotics improves outcomes, especially for unstable or nonadherent patients, has never been empirically evaluated. In a 14-site, 2-year, partly manufacturer-supported, randomized, controlled study, researchers compared the effectiveness of long-acting, biweekly injectable risperidone (25-50 mg) and equivalently dosed oral antipsychotics in 369 Veterans Affairs (VA) patients with unstable schizophrenia (mean age, 50; 95% hospitalized currently or within the previous 2 years, 64% with poor medication adherence, 37% with substance use problems).

Both treatment groups had similarly declining follow-up rates over time and similar duration of adherence to the randomized treatment. Of the oral medication group, 12% switched to the depot injectable drug; of the depot group, 32% to 40% took concomitant oral antipsychotics. The groups had similar rates of hospitalization, time to first hospitalization, and subsequent VA service use. No clinical differences were seen in positive and negative symptoms, quality of life, addiction

severity, or global mental health status. Findings were unchanged in analyses adjusting for crossover treatment and covariates.

Comment: These surprising negative findings will spur controversy in community mental health settings, as many clinicians believe that injectable antipsychotics improve outcomes for nonadherent, unstable patients with schizophrenia. The study was not perfect (e.g., patients were older veterans; some were previously medication-adherent; many likely had intrinsically unstable disease, which is less amenable to treatment; and the study was not powered enough to detect small differences). Still, these findings have clear policy implications because the two treatments seem to have highly similar outcomes and related costs. Individual nonadherent patients might profit from a switch to injectable medication, but the findings suggest that routinely switching is unlikely to generally improve outcomes or, more important for policy decisions, save money.

<http://psychiatry.jwatch.org/cgi/content/full/2011/302/1>

## NATIONAL STUDY OF SUICIDE IN ALL PEOPLE WITH A CRIMINAL JUSTICE HISTORY

Roger T. Webb, PhD & Colleagues - Arch Gen Psychiatry. 2011

**Context** Previous research has focused on suicide among male prisoners and ex-prisoners, but little is known about risk in the wider offender population.

**Objective** To examine suicide risk over 3 decades among all people processed by a national criminal justice system.

**Design** Nested case-control study.

**Setting** The whole Danish population.

**Participants** Interlinked national registers identified all adult suicides during 1981 to 2006 according to any criminal justice system contact since 1980. Exposure was defined according to history of criminal justice adjudication, up to and including each subject's last judicial verdict before suicide (or date of matching for controls). There were 27 219 suicides and 524 899 controls matched on age, sex, and time, ie, controls were alive when their matched case died.

**Main Outcome Measure** Suicide.

**Results** More than a third of all male cases had a criminal justice history, but relative risk against the general population was higher for women than men. Independent effects linked with criminal justice exposure persisted with confounder adjustment. Suicide risk was markedly elevated with custodial sentencing, but the strongest effects were with sentencing to psychiatric treatment and with charges conditionally withdrawn. Risk was raised even in people with a criminal justice history but without custodial sentences or guilty verdicts. It was especially high with recent or frequent contact and in people charged with violent offenses.

**Conclusions** We examined a section of society in which major health and social

problems frequently coexist including offending, psychopathology, and suicidal behavior. The need for developing more far-reaching national suicide prevention strategies is indicated. In particular, improved mental health service provision is needed for all people in contact with the criminal justice system, including those not found guilty and those not given custodial sentences. Our findings also suggest that public services should be better coordinated to tackle co-occurring health and social problems more effectively.

<http://archpsyc.ama-assn.org/cgi/content/abstract/68/6/591?>

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## A MULTIVARIATE TWIN STUDY OF OBSESSIVE-COMPULSIVE SYMPTOM DIMENSIONS

Alessandra C. Iervolino, PhD & Colleagues - Arch Gen Psychiatry. 2011

**Context** Obsessive-compulsive disorder (OCD) is clinically heterogeneous, but it is unclear whether this phenotypic heterogeneity reflects distinct, or partially distinct, etiologic mechanisms.

**Objective** To clarify the structure of the genetic and environmental risk factors for the major symptom dimensions of OCD.

**Design** Self-report questionnaires and multivariate twin model fitting.

**Setting** General community.

**Participants** A total of 4355 female members of the Twins UK adult twin register.

**Main Outcome Measures** Scores on the Obsessive-Compulsive Inventory-Revised and 5 of its subscales (checking, hoarding, obsessing, ordering, and washing).

**Results** A common pathway model did not fit the data well, indicating that no single latent factor can explain the heterogeneity of OCD. The best-fit multivariate twin model was an independent pathway model, whereby both common and unique genetic and/or environmental factors contribute to the etiology of each symptom dimension. The hoarding

dimension had the lowest loading on the common factor and was more influenced by specific genetic effects (54.5% specific). With the exception of hoarding, most of the genetic variance was due to shared genetic factors (ranging from 62.5% to 100%), whereas most of the nonshared environmental variance was due to dimension-specific factors.

**Conclusions** Obsessive-compulsive disorder is unlikely to be an etiologically homogeneous condition. There is substantial etiologic overlap across the different OC symptom dimensions, but dimension-specific genetic, and particularly nonshared environmental, factors are at least as important. Hoarding shares the least amount of genetic liability with the remaining symptom dimensions. The results have implications for the current deliberations regarding OCD and the inclusion of a putative hoarding disorder in DSM-5.

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[http://archpsyc.ama-assn.org/  
cgi/content/abstract/68/6/637?](http://archpsyc.ama-assn.org/cgi/content/abstract/68/6/637?)  
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## RELATIONSHIP BETWEEN HOUSEHOLD INCOME AND MENTAL DISORDERS

### Findings From a Population-Based Longitudinal Study

Jitender Sareen, MD, FRCPC & Colleagues - Arch Gen Psychiatry. 2011

**Context** There has been increasing concern about the impact of the global economic recession on mental health. To date, findings on the relationship between income and mental illness have been mixed. Some studies have found that lower income is associated with mental illness, while other studies have not found this relationship.

**Objective** To examine the relationship between income, mental disorders, and suicide attempts.

**Design** Prospective, longitudinal, nationally representative survey.

**Setting** United States general population.

**Participants** A total of 34 653 noninstitutionalized adults (aged 20 years) interviewed at 2 time points 3 years apart.

**Main Outcomes** Lifetime DSM-IV Axis I and Axis II mental disorders and lifetime suicide attempts, as well as incident mental disorders and change in income during the follow-up period.

**Results** After adjusting for potential confounders, the presence of most of the lifetime Axis I and Axis II mental disorders was associated with lower levels of income. Participants with household income of less than \$20 000 per year were at increased risk of

incident mood disorders during the 3-year follow-up period in comparison with those with income of \$70 000 or more per year. A decrease in household income during the 2 time points was also associated with an increased risk of incident mood, anxiety, or substance use disorders (adjusted odds ratio, 1.30; 99% confidence interval, 1.06-1.60) in comparison with respondents with no change in income. Baseline presence of mental disorders did not increase the risk of change in personal or household income in the follow-up period.

**Conclusions** Low levels of household income are associated with several lifetime mental disorders and suicide attempts, and a reduction in household income is associated with increased risk for incident mental disorders. Policymakers need to consider optimal methods of intervention for mental disorders and suicidal behavior among low-income individuals.

<http://archpsyc.ama-assn.org/cgi/content/abstract/68/4/419?>

# DEEP BRAIN STIMULATION OF THE NUCLEUS ACCUMBENS FOR TREATMENT-REFRACTORY OBSESSIVE-COMPULSIVE DISORDER

Denys D et al. \_ Arch Gen Psychiatry 2010 Oct

**Deep** brain stimulation (DBS) for refractory obsessive-compulsive disorder (OCD) usually targets behavior-generating systems like the ventral striatum or its fibers as they pass through the anterior limb of the internal capsule. These researchers addressed dysfunctional reward systems by targeting the nucleus accumbens in 16 patients with refractory OCD (illness duration, 8-46 years; 3-13 medication trials; 1-8 cognitive-behavioral therapy [CBT] trials).

Electrodes were implanted bilaterally in the nucleus accumbens. The study had three phases. The 8-month, open-label phase 1 involved active stimulation; weekly CBT started at week 8. In the double-blind, cross-over phase 2, patients were randomized to active or sham stimulation for 2 weeks and then the opposite condition for another 2 weeks. Phase 3 provided open-label active stimulation for 1 year.

At 21 months, mean OCD symptoms decreased by 52%; nine patients were responders (defined as symptom decrease, 35%), with a mean symptom decrease of 71%. In patients first receiving sham stimulation during phase 2, symptoms worsened rapidly and then improved

significantly during active treatment. In contrast, in patients first receiving active stimulation, the difference between active and sham treatment was not significant, possibly because the group showed slightly worsened scores at the start of phase 2 and had a higher proportion of nonresponders. Anxiety- and depression-rating scale scores significantly decreased with active treatment. Patients with perfectionism, hoarding, or symmetry needs responded less than other patients.

**Comment:** OCD symptoms may result from an interaction between behavior generation and excessive depression and anxiety in response to OCD cues. Interrupting particular systems may be effective for specific OCD subtypes, although the exact syndromes that respond best to DBS in the striatum versus in the limbic system remain to be defined. As more is learned about the interventions best suited to specific refractory disorders, DBS will become more useful.

<http://psychiatry.jwatch.org/cgi/content/full/2010/1108/3>

## ZOLPIDEM AND ZOPICLONE IMPAIR SIMILARLY MONOTONOUS DRIVING PERFORMANCE AFTER A SINGLE NIGHTTIME INTAKE IN AGED SUBJECTS

Bocca M-L et al. - *Psychopharmacology* (Berl) 2011 Apr

**Zolpidem** has been shown to lack residual effects on driving the next day in young and middle-aged recipients. However, information is sparse on its effects on driving in older individuals, even though use of hypnotics increases with age. In a double-blind, crossover study, researchers examined how a single nighttime dose of zolpidem, another hypnotic, or benzodiazepine affected driving the next morning in 16 healthy subjects (8 women) aged 55 to 65 years.

Subjects lacked sleep disorders, histories of substance abuse, or impaired vision. On separate occasions at least 2 weeks apart, the subjects took zolpidem 10 mg, the hypnotic zopiclone 7.5 mg, the benzodiazepine flunitrazepam 1 mg, or placebo at night. The next day, they were tested in a driving simulator in urban and monotonous driving conditions.

All subjects slept during the experimental nights, as verified by polysomnography. Compared with placebo, zolpidem was associated with next-day significantly greater difficulty in keeping the car in the lane and maintaining a constant speed.

Impairment was similar after zopiclone, but was less with flunitrazepam, which the investigators attributed to the low dosage. The morning after taking zolpidem, subjects reported lower alertness; 11 had detectable zolpidem blood levels.

**Comment:** In this small study, researchers did not compare driving performance in people of different ages and examined effects of only acute, not regular, medication use. Despite these limitations, the results raise concerns about possible impairment in routine, monotonous driving in individuals in their 50s or 60s starting on zolpidem or taking it as needed. Fortunately, subjects were aware of their diminished alertness. Clinicians should consider prescribing a lower starting dose of zolpidem (5 mg) even in patients younger than 65 and should warn patients against driving if they feel sedated.

[http://psychiatry.jwatch.org/cgi/content/full/2011/411/2?q=etoc\\_jwpsych](http://psychiatry.jwatch.org/cgi/content/full/2011/411/2?q=etoc_jwpsych)



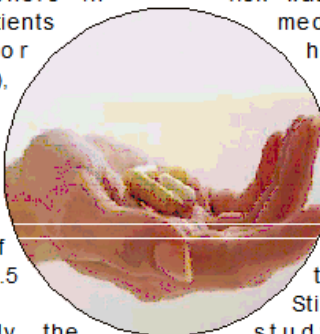
## ILLNESS RISK FOLLOWING RAPID VERSUS GRADUAL DISCONTINUATION OF ANTIDEPRESSANTS

Baldessarini RJ et al - Am J Psychiatry 2010

### Going slower is better.

Patients' risks for relapse increase when lithium or antipsychotic medications are discontinued rapidly rather than gradually. To compare rapid (1-7 days) versus slow (14 days) discontinuation of antidepressants, researchers in Sardinia followed 398 patients with recurrent major depressive disorder (n=224), panic disorder (n=75), bipolar II disorder (n=62), or bipolar I disorder (n=37). Follow-up lasted at least 1 year (mean, 2.8 years; mean length of antidepressant treatment, 8.5 months).

In this observational study, the treating clinicians or the patients had chosen to discontinue medications when patients were clinically well; antidepressants were withdrawn rapidly in 188 patients and gradually in 210. Rapid discontinuation was associated with a significantly shorter time to relapse than gradual discontinuation (median, 3.6 vs. 8.4 months). The authors estimated that time to relapse after rapid discontinuation was only 25% of the average time to earlier relapses in the same patients. The findings were most evident for bipolar I and panic disorders.



After rapid discontinuation, the intervals preceding relapse were similar among different drug types, but after gradual discontinuation, time to relapse was substantially longer with tricyclics than with modern antidepressants. Relapse risk was the least pronounced for medications with prolonged half-lives and was not associated with antidepressant dose, duration of illness or treatment, or concurrent treatment.

**Comment:** Several uncertainties remain, and the study needs replication. Still, these findings align with study results on other psychotropics. Rapid discontinuation substantially increases relapse risks and shortens relapse latencies. Clinicians opting to discontinue antidepressants, particularly short-acting serotonin reuptake inhibitors, should plan to taper over weeks to months. As an editorialist notes, clinicians should forewarn patients who decide to abruptly discontinue their medications, especially pregnant women, of these risks.

<http://psychiatry.jwatch.org/cgi/content/full/2010/903/1>

## LACK OF EVIDENCE FOR THE EFFICACY OF MEMANTINE IN MILD ALZHEIMER DISEASE

Schneider LS et al. Arch Neurol April 2011

**Memantine** is an N-methyl-D-aspartate receptor antagonist that has been approved in the U.S. and Europe as a treatment for moderate-to-severe Alzheimer disease (AD). It is also frequently used off-label for mild AD. To determine whether such use is warranted, researchers conducted a meta-analysis of randomized, double-blind, placebo-controlled,

memantine trials that included patients with mild AD. They identified three such trials, each lasting 24 weeks: two U.S. studies of patients with Mini-Mental State Examination (MMSE) scores of 10 to 22 (1 study allowed concurrent use of cholinesterase

inhibitors) and a European study of patients with MMSE scores of 11 to 23. Of the 1128 participants in these trials, 431 (38%) had mild AD (MMSE score, 20-23).

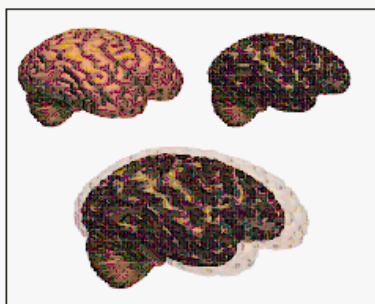
In none of the trials (either individually or combined) did patients specifically with mild AD derive a significant benefit from memantine over placebo in cognitive function, global functioning, activities of daily living, or observed behavior. Given that placebo recipients with mild AD tended to

improve on cognitive measures and to remain stable on global measures, drug effects, if any, would have been difficult to discern in trials of this size and duration.

**Comment:** This study involved a clever re-examination of data from six memantine trials included in two previous manufacturer-funded meta-analyses that reported positive

findings. A meta-analysis from Europe (Alzheimers Dement 2007; 3:7) specifically excluded patients with mild AD, and the other, from the U.S. (Dement Geriatr Cogn Disord 2007; 24:20), collectively analyzed patients at all

disease stages. The current, non-industry-supported meta-analysis, which focused specifically on patients with mild AD, documented no advantage of memantine over placebo on any analyzed measures. Off-label use of memantine in patients with mild AD, which is common in clinical practice, is simply not supported by these newly published data.



<http://neurology.jwatch.org/cgi/content/full/2011/517/1>

## TREATMENT FOR PTSD RELATED TO CHILDHOOD ABUSE: A RANDOMIZED CONTROLLED TRIAL

Cloitre M et al - Am J Psychiatry 2010

**Scores** of treatment studies have investigated post-traumatic stress disorder (PTSD) associated with trauma in adulthood. Far fewer have focused on PTSD resulting from childhood abuse, which, some researchers suggest, results in "complex PTSD," frequently associated with personality disorders and difficult to treat. In a randomized controlled trial, investigators enrolled 104 women with histories of early and chronic childhood abuse. They compared a combination treatment consisting of a preparatory phase of skills training in emotion regulation and interpersonal effectiveness followed by exposure (skills training/exposure) versus two control conditions: supportive counseling followed by exposure (support/exposure) and skills training followed by supportive counseling (skills training/support).

Treatments consisted of 16 weekly sessions, 8 in each phase. Skills training resembled dialectical behavior therapy (DBT) followed by interpersonal skills practice. Exposure involved review of narratives of traumatic events. Exclusions were for acute suicidality, untreated bipolar disorder, psychosis, cognitive impairment, and substance abuse. Overall, 88% of patients had axis I comorbidities, 54% had axis II

comorbidities, and adult domestic violence was reported by 60%.

Across treatments, completion ranged from 61% to 85%, with the fewest dropouts in the skills training/exposure group. Intent-to-treat analyses showed 3- and 6-month benefits for skills training/exposure on PTSD symptoms, mood, and interpersonal problem inventories. By the 6-month follow-up, some patients showed symptom exacerbation, ranging from a cumulative 3.6% in the skills training/exposure group to 31.3% in the support/exposure group.

**Comment:** Although skills training/exposure produced the best results, several other studies have not shown that similar treatment combinations have results superior to either modality alone. Replication by other groups using these investigators' specific manuals and techniques is essential. Meanwhile, clinicians may find that the careful melding of DBT and exposure elements, as used in this approach, can be helpful in treating patients with complex PTSD.

<http://psychiatry.jwatch.org/cgi/content/full/2010/823/3>



## VIOLENCE AGAINST WOMEN BY THEIR INTIMATE PARTNER DURING PREGNANCY AND POSTNATAL DEPRESSION: A PROSPECTIVE COHORT STUDY

Ludermir AB et al - Lancet 2010

**Intimate** partner violence affects 4% to 8% of pregnant women in the U.S. and is associated with postnatal depression. However, the effects of psychological violence on postpartum depression are unclear. To assess whether intimate partner violence during pregnancy, especially psychological abuse, is associated with later postnatal depression, researchers prospectively followed pregnant, mostly low-income women (age range, 18-49) enrolled in primary-care clinics in northeast Brazil through the postpartum period. Interviews took place during the third trimester and an average of 8 months later.

Of 1045 women with complete data, 321 (31%) reported partner violence during pregnancy. Psychological violence (insults, humiliation, intimidation, or threats) was most common (294 women [28% of the sample]); 123 women reported physical violence, and 60 reported sexual violence, typically along with psychological violence. Postpartum depressive symptoms were reported by 270 women (26%). The risk for postpartum depressive symptoms was highest in women reporting physical or

sexual violence plus psychological violence. Risk for depressive symptoms increased progressively with greater frequency of psychological violence (from 18% of women with no psychological abuse to 63% in those most frequently abused). Even in the absence of physical or sexual violence and after adjustment for potentially confounding factors, psychological violence, especially when more frequent, significantly increased depression risk.

**Comment:** This study used a self-report scale, not DSM-IV diagnoses, to assess depressive symptoms postpartum, and several confounders (e.g., low levels of education and social support) were associated with both partner violence and postnatal depression. Nevertheless, these results underscore the importance of asking pregnant women about intimate partner violence, including psychological abuse, which often receives less attention than physical or sexual violence.

[http://psychiatry.jwatch.org/  
cgi/content/full/2010/913/2](http://psychiatry.jwatch.org/cgi/content/full/2010/913/2)

## CHILDHOOD ADVERSITIES AS RISK FACTORS FOR ONSET AND PERSISTENCE OF SUICIDAL BEHAVIOUR

Bruffaerts R et al - Br J Psychiatry 2010

**Childhood** adversity has been consistently associated with adult suicidality. However, little evidence exists about whether the type or number of adversities affects the risk for onset of suicidality, whether the risk varies over the life span, whether adversities predict persistence or transition from ideation to attempt, and whether these effects are similar worldwide. These researchers reanalyzed data from the cross-sectional World Mental Health surveys in 21 countries (109,377 participants) to examine the relation between nine adversities (e.g., sexual and physical abuse, parental death, financial adversity) and suicidal ideation and suicide attempt.

Of the respondents, 2.7% reported lifetime suicide attempt and 9.4% reported lifetime suicidal ideation. Physical and sexual abuse and neglect had the greatest effects on ideation and attempt. Overall, the risk for suicidality increased with a higher number of reported adversities, but at a decreasing rate. The risk for onset of suicide attempts was significant at all ages but was greatest between ages 4 and 12 years (median odds ratio [OR], 3.8), with

the highest risks among those who experienced sexual or physical abuse (ORs, 10.9 and 6.3, respectively). Only physical abuse and sexual abuse were associated with persistence of most suicidal behaviors. All associations remained significant after adjustment for the statistically significant effect of having a mental disorder.

**Comment:** Despite the use of retrospective data, this multinational, population-based analysis clearly documents the powerful role of childhood adversities in the onset and persistence of suicidal behavior. These risk factors are similar in magnitude to that of having a mental disorder,

which appears to play only a minor role in the association between adversities and suicide. The findings are consistent with a growing interest in developing psychotherapeutic techniques that would reduce or eliminate suicidal ideation, planning, and intent by exploring the psychological determinants of suicidality, rather than by treating the mental disorder that supposedly leads to suicidality.

<http://psychiatry.jwatch.org/cgi/content/full/2010/823/4>



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## METHOD OF ATTEMPTED SUICIDE AS PREDICTOR OF SUBSEQUENT SUCCESSFUL SUICIDE: NATIONAL LONG TERM COHORT STUDY

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Runeson B et al - BMJ 2010

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**Predicting** suicide, a very infrequent event, is extremely difficult. The best predictor of successful suicide is a history of a previous attempt. However, the hypothesis that more-severe methods of attempted suicide confer greater risk has been infrequently studied. Now, researchers in a prospective cohort study have analyzed Swedish hospital and death registries on 48,649 individuals hospitalized between 1973 and 1982 after a suicide attempt (84% by poisoning).

The researchers controlled for relevant demographics and psychiatric disorders (i.e., affective, psychotic, or other) and compared various suicide-attempt methods to poisoning, the index method. During follow-up (range, 21-31 years), 11.8% of individuals died by suicide, most using the method of their original attempt. Previous attempt methods that posed the highest risks for later completed suicide were hanging, strangulation, or suffocation (hazard ratio [HR], 6.2) followed by drowning, jumping, and shooting (HRs, 3.2-4.0). Cutting and other methods conferred a risk similar

to poisoning. Over half the individuals in the highest-risk group ultimately committed suicide, 87% within 1 year of the attempt. The diagnosis with the highest independent risk was psychosis (HR, 2.5); 84% of psychotic patients who tried to hang themselves died later by suicide.

**Comment:** Findings from this study, the largest and most representative study on this topic, strongly suggest that certain suicide-attempt methods confer a great risk for future suicide. Study limitations include imprecise psychiatric diagnostic information, the absence of information on other risk factors, and the exclusion of suicide attempters who were not psychiatrically hospitalized. Nonetheless, individuals, especially those with psychosis, who attempt to kill themselves by hanging, drowning, shooting, or jumping are at extremely high risk for completed suicide.

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[http://psychiatry.jwatch.org/  
cgi/content/full/2010/830/1](http://psychiatry.jwatch.org/cgi/content/full/2010/830/1)

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## USE OF ANTIEPILEPTIC DRUGS IN EPILEPSY AND THE RISK OF SELF-HARM OR SUICIDAL BEHAVIOR

Andersohn F et al - Neurology

In 2008, the FDA issued an alert about the increased suicide risk with antiepileptic drugs (AEDs) in epilepsy patients, based on a meta-analysis that did not determine differential risk of individual AEDs. Now, researchers have conducted a nested case-control study within a cohort of 44,300 epilepsy patients prescribed AEDs between 1989 and 2005 to examine risk in four drug categories - barbiturates, conventional AEDs, "new" AEDs with low potential for causing depression (lamotrigine, gabapentin, pregabalin, oxcarbazepine), and new AEDs with high depression potential (levetiracetam, tiagabine, topiramate, vigabatrin). The 453 cases with occurrence of self-harm or suicidal behavior (defined by codes in U.K. electronic medical records) were matched with 8962 controls by age and sex. Epilepsy types were similar in cases and controls, but cases had greater psychiatric comorbidity. Analyses controlled for psychiatric comorbidity and epilepsy type. Only current use of new AEDs with high depression risk was associated with significantly increased risk for suicidal behavior and self-harm, compared with no AED use in the year before suicidal

behavior/self-harm. When individual AEDs were analyzed, only levetiracetam had an increased risk. However, only six patients taking depressogenic new AEDs had suicidal behaviors (levetiracetam, 2; topiramate, 2; vigabatrin, 2).

**Comment:** The FDA warning might have been excessive: Only a few AEDs may be associated with suicidality in epilepsy patients. The authors and commentators note that the findings are not definitive. Some drug subgroups were very small, epilepsy diagnoses were not fully validated, patients receiving newer AEDs might have had refractory epilepsy, and post-2005 data on newer AEDs might be more extensive. The study does demonstrate that electronic medical records can help researchers analyze rare risk factors in large groups of patients.

The study does not address the psychiatric use of AEDs, although researchers in another study associated the risk for suicide or self-harm more with the diagnosis than with the drug. In any case, psychiatrists who treat patients with epilepsy should be aware of these possible associations.

<http://psychiatry.jwatch.org/cgi/content/full/2010/903/2>

## HIGH DOSE D-SERINE IN THE TREATMENT OF SCHIZOPHRENIA

Kantrowitz JT et al - Schizophr Res 2010

**Although** most antipsychotic drugs are based on the dopamine model of schizophrenia, phencyclidine (which induces psychotic symptoms) modulates N-methyl-D-aspartate (NMDA) receptors. In some studies, an agonist at the NMDA site, D-serine, has demonstrated positive results at 30 mg/kg/day in patients with schizophrenia. To explore the relative safety and efficacy of various D-serine doses, researchers examined the effects of 30 mg/kg/day, 60 mg/kg/day, and 120 mg/kg/day in 42 patients with schizophrenia or schizoaffective disorder who were stabilized on antipsychotics (>450 mg/day of chlorpromazine equivalents). The senior author has intellectual property rights to this therapeutic approach.

Patients were in their early 40s, were predominately male, and had significant cognitive deficits at baseline. In the 4-week, open-label trial, researchers assessed positive and negative symptoms biweekly and obtained neuropsychological testing before and after the study. Some patients participated in more than one dosing study, but more than 6 months lapsed between trials. All doses produced significant improvement in general schizophrenia symptoms, and all symptom subscales improved with the highest dose, but neurocognitive function improved on only the two higher doses.

Thirty-six percent of patients were rated as at least mildly improved globally, with no difference among dosages. Levels of D-serine increased over the 4 weeks, were greater at the higher dosages, and correlated with improvement. There were few important safety issues (at 120 mg, insomnia and gastrointestinal distress after one dose, and asymptomatic transaminitis).

**Comment:** These encouraging results require replication in a double-blind, placebo-controlled, long-term study, once the most effective dose is identified. Whether these effects are specific to patients with schizophrenia or would benefit those with other neuropsychiatric disorders (bipolar, anxiety, or cognitive disorders) should be explored.

Because several supplements and drugs sound similar to D-serine, the following information, obtained from communications with the senior author, is provided for clarification: D-serine is not yet readily available, and its long-term safety has not been established. Phosphatidylserine contains L-serine rather than D-serine. D-cycloserine (an antituberculosis drug) is somewhat similar to D-serine, can be given at much lower dosages (e.g., 50 mg/day), but does not seem as effective.

<http://psychiatry.jwatch.org/cgi/content/full/2010/903/3>

## NEUROPROTECTIVE EFFECTS OF COGNITIVE ENHANCEMENT THERAPY AGAINST GRAY MATTER LOSS IN EARLY SCHIZOPHRENIA: RESULTS FROM A 2-YEAR RANDOMIZED CONTROLLED TRIAL

Eack SM et al - Arch Gen Psychiatry 2010

**Progressive** loss of neurons, ventricular enlargement, frontotemporal hypofunction, and impaired white matter integrity have been well described in schizophrenia and are associated with impaired memory and executive function. These investigators randomized 53 patients with onset of schizophrenia or schizoaffective disorder within the previous 8 years (mean illness duration, 3.2 years) to a 2-year course of cognitive-enhancement therapy (CET) or a control therapy (enriched supportive therapy [EST]) and performed magnetic resonance imaging at baseline and annually.

With CET, pairs of patients received 60 hours of weekly computer-based neurocognitive training focused on attention, processing speed, memory, and executive function; after a few months, three to four patient pairs formed groups that addressed social cognition, nonverbal communication, emotion management, insight, perspective taking, and social gist abstraction in 45 weekly sessions, with regular homework assignments. EST involved biweekly individual therapy directed at stress reduction, illness management, recognition of relapse signs, and coping strategies. Medications were

similar across groups.

Gray matter showed significantly less loss, and even preservation, in the left hippocampus, parahippocampal gyrus, and fusiform gyrus in patients who received CET, especially in scans conducted at the end of treatment, compared with EST recipients. CET recipients also had significant increases in the left amygdala compared with EST recipients, who showed amygdala volume losses. The apparent neuroprotective effects of CET correlated with enhanced neurocognition.

**Comment:** Improved cognition and enhanced ability to recognize and respond appropriately to social cues may be mediated by CET's effect in reducing (even reversing, in the amygdala) neurodegenerative changes in schizophrenia. The results suggest that exercising the brain in a specific manner improves brain function. Structured therapies like CET should be a component of rehabilitation in all patients with schizophrenia, particularly early in the illness when changes in the brain may be reversible.

<http://psychiatry.jwatch.org/cgi/content/full/2010/823/1>



## SOCIAL RISK OR GENETIC LIABILITY FOR PSYCHOSIS? A STUDY OF CHILDREN BORN IN SWEDEN AND REARED BY ADOPTIVE PARENTS

Wicks S et al - Am J Psychiatry Aug 2010

**Decades** ago, now-classic follow-up studies of adopted-away children of schizophrenic mothers clinched the association between genetics and the etiology of schizophrenia. Using large Swedish databases, investigators have now revisited the issue, looking for both genetic and potential environmental contributions to the risk for psychosis.

Researchers examined data on 13,163 adoptees born between 1955 and 1984; 230 were admitted at some-point for a nonaffective psychosis. Among adoptees whose biological parents had no histories of inpatient care for psychosis, risk for nonaffective psychosis was raised with socioeconomic disadvantage, but not significantly so (hazard ratios: adoptive parental unemployment, 2.0; being raised in single-parent households, 1.2; living in apartments, 1.3). The HR for having a biological liability alone (i.e., no socioeconomic disadvantage) was associated with a significantly increased HR of 4.7. Having both biological vulnerability and socioeconomic disadvantage created the greatest risks for psychosis, with HRs of 15.0 for adoptive parental unemployment, 10.3 for single-parent household, and 5.7 for apartment living.

**Comment:** These epidemiological data suggest independent biological and socio-environmental contributions to the vulnerability to psychosis, but they leave numerous questions unanswered. For example, although the analyses excluded adoptions by grandparents and siblings, some children might have been adopted by other close biological relatives, and these families might be at increased risk for both psychosis and socioeconomic disadvantage. Mechanisms linking socioeconomic disadvantage to increased rates of psychosis in vulnerable children remain to be elucidated. Environmental stressors could trigger biological events in genetically (and epigenetically) vulnerable individuals; or, perhaps, other intermediate events such as increased stimulant or marijuana abuse might contribute to psychosis risk. Clinicians seeing children whose biological parents have schizophrenia and who are growing up with socioeconomic disadvantages should be particularly alert to the risk for developing psychosis.

[http://psychiatry.jwatch.Org/  
cgi/content/full/2010/913/3](http://psychiatry.jwatch.Org/cgi/content/full/2010/913/3)

## STRESS COPING STIMULATES HIPPOCAMPAL NEUROGENESIS IN ADULT MONKEYS

Lyons DM et al - Proc Natl Acad Sci U S A 2010 Jul 30

**Animal** studies have shown increased hippocampal neurogenesis with antidepressant use (Proc Natl Acad Sci U S A 2001; 98:12796), but less is known about the hippocampal effects of coping with naturally occurring stress, which would have implications for nonpharmacological psychiatric treatments. To test the effect of coping with stress on hippocampal neurogenesis and hippocampal-related behaviors, these researchers used an animal model that mimics coping with naturally occurring environmental stress. Twelve male monkeys were randomized to either living for 18 months with the same male partner (nonstressed control group) or to six 3-month sessions, in which monkeys spent the first 3 weeks in isolation and the last 9 weeks with a new male partner (stressed experimental group). The experimental condition is similar to these monkeys' typical social environment, in which males compete for inclusion in groups with females. To measure hippocampal function, researchers trained the monkeys in a spatial learning task involving food retrieval. During the last session of the experiment, all monkeys received a marker for neurogenesis (BrdU). At study's end, monkey brains were examined for uptake of BrdU (a measure

of new cell formation), uptake of a marker for mature neurons (NeuN), and gene expression. Compared with controls, experimental monkeys exhibited significantly higher spatial learning and 44% more hippocampal neurogenesis, measured by the number of neurons double-labeled with BrdU and NeuN. Activation of five genes related to neuronal functioning was significantly different between cases and controls. In both groups, more than 85% of new cells stained positive for NeuN, an indication that the new cells had become mature neurons.

**Comment:** The neurogenesis in these primates suggests that coping with stress might also produce neurogenesis in people. The findings also suggest that nondrug stress-coping interventions for mood and anxiety disorders would lead to hippocampal neurogenesis, similar to that seen with antidepressant use. Clinicians can be encouraged that their nondrug interventions may well be producing improved hippocampal morphology and function similar to that seen with pharmacological agents.

<http://psychiatry.jwatch.org/cgi/content/full/2010/913/1>

## META-ANALYTICAL COMPARISON OF VOXEL-BASED MORPHOMETRY STUDIES IN OBSESSIVE-COMPULSIVE DISORDER VS OTHER ANXIETY DISORDERS

Radua J et al - Arch Gen Psychiatry 2010 Jul

**People** with obsessive-compulsive disorder (OCD) experience considerable anxiety when they attempt to resist compulsions, but does this anxiety drive their obsessions and compulsions? Researchers addressed the question by analyzing data from 26 voxel-based morphometry studies (OCD, 14; panic disorder, 5; post-traumatic stress disorder [PTSD], 6; various anxiety disorders, 1) involving 639 patients with anxiety disorders (430 with OCD) and 737 healthy controls.

The researchers controlled for antidepressant use and age. Other medication use and patient sex did not significantly differ among the different anxiety diagnoses. Compared with controls, the patients - regardless of diagnosis - had smaller regional gray matter volumes bilaterally in the dorsomedial frontal and anterior cingulate gyri. Compared with controls, patients with OCD had greater gray matter volumes bilaterally in the lenticular (primarily, the ventral anterior putamen) and caudate nuclei, whereas patients with panic disorder or PTSD had smaller gray matter volume in the

left lenticular nucleus (primarily, the ventral anterior putamen).

**Comment:** The results of this meta-analysis suggest that OCD and other anxiety disorders share activation sites, but that OCD differs from other anxiety disorders in its association with an apparent expansion of the basal ganglia, a finding confirmed in functional neuroimaging studies and in a study correlating basal ganglia size with OCD severity. The neural pathway for producing anxiety may be the same as for the system producing the behaviors that lead to anxiety in OCD, but this latter system appears to be affected differentially in OCD and other anxiety disorders. Because the two sets of disorders also differ in their specific responses to selective serotonin reuptake inhibitors and deep brain stimulation of the caudate, it seems appropriate to consider them different but related disorders, to study them separately, and to treat them differently.

[http://psychiatry.jwatch.org/  
cgi/content/full/2010/830/3](http://psychiatry.jwatch.org/cgi/content/full/2010/830/3)

## EFFECT OF NALTREXONE PLUS BUPROPION ON WEIGHT LOSS IN OVERWEIGHT AND OBESE ADULTS (COR-I): A MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 3 TRIAL

Greenay FL et al - Lancet Aug 2010

**Obesity** is a major public health problem, common in psychiatric patients and individuals taking psychotropic medications, and difficult to treat medically. Researchers conducted a 56-week, multicenter, industry-sponsored, randomized, controlled trial to examine the efficacy of a combination of two medications already used in psychiatry and addiction medicine - sustained-release bupropion and sustained-release naltrexone. The 1742 participants had either a body-mass index (BMI) of 30 to 45 kg/m<sup>2</sup> or BMI of at least 27 kg/m<sup>2</sup> with dyslipidemia or hypertension (mean age, 44; 85% women). Individuals with "serious psychiatric illness" or major medical problems were excluded. Participants were randomized to one of three treatment groups: 32 mg naltrexone plus 360 mg bupropion (32N+B); 16 mg naltrexone plus 360 mg bupropion (16N+B); or matched placebo. Advice about exercise and diet was provided, but these were not monitored. Approximately 50% of participants (870) completed treatment.

Among the 1453 participants with baseline and at least one postbaseline weight measurements, active treatment (especially 32N+B) was superior to placebo in producing

weight loss starting at week 4, with maximum weight loss achieved at 28 to 36 weeks. Active treatment produced significantly greater mean change in body weight than placebo (32N+B, -6.1%; 16N+B, -5.0%; placebo, -1.3%) and mean amount of weight lost (6.1 kg, 4.9 kg, and 1.4 kg). The 32N+B regimen tripled the likelihood of losing 5% or 10% of body weight. Combined treatment was associated with favorable health outcomes, improved control of eating, and reduction in food cravings.

**Comment:** This promising new approach produced results comparable or superior to those achieved with other weight loss medications (e.g., orlistat). Although no participants had serious psychiatric illness, the results are promising for psychiatry patients, as bupropion and naltrexone are already used for some psychiatric conditions and addiction disorders. This study, along with preclinical studies showing synergism of bupropion and naltrexone in midbrain dopaminergic areas, adds support to the conceptualization of obesity as an addiction.

[http://psychiatry.jwatch.org  
/cgi/content/full/2010/913/4](http://psychiatry.jwatch.org/cgi/content/full/2010/913/4)



## COGNITIVE BEHAVIORAL THERAPY VS RELAXATION WITH EDUCATIONAL SUPPORT FOR MEDICATION-TREATED ADULTS WITH ADHD AND PERSISTENT SYMPTOMS: A RANDOMIZED CONTROLLED TRIAL

Safren SA et al - JAMA, Aug 2010

Of the estimated 4.4% of U.S. adults with ADHD, many respond to medication but continue to have symptoms. This therapy add-on study involved 86 patients (mean age, 43) who had at least mildly and persistently symptomatic ADHD initially diagnosed in childhood, were on stable psychotropic medication regimens, and lacked major psychiatric comorbidities. Participants were randomized to 12 sessions of individual cognitive-behavioral therapy (CBT) or relaxation training plus education. CBT modules focused on psychoeducation regarding ADHD and training in organizing, planning, and problem solving; skills to reduce distractibility; and cognitive restructuring (thinking adaptively in distress-causing situations). Two sessions were boosters or focused on procrastination (n=40) or support from significant others (n=27). The control treatment consisted of one psychoeducation session, six on progressive muscle relaxation, four on applying relaxation to ADHD, and one wrap-up.

Although both groups improved, the CBT group showed more improvement posttreatment, with moderately better treatment-effect sizes. Depending on the scale, 53% to 67% of the CBT group

responded, roughly double the response rates in the control group. In both groups, mean Clinical Global Impressions scale ratings declined from moderate severity at baseline (CBT, 4.74; relaxation and education, 4.63) to mild illness posttreatment (3.20 and 3.73). At 6- and 12-month follow-ups, gains by partial or full responders in both groups were generally maintained.

**Comment:** Given the distress and impairment associated with ADHD in adulthood, additional options for treatment are highly desirable. This excellent first-step study demonstrates the value of individually administered add-on therapy. CBT appeared to be moderately superior to relaxation and education. Recently, group metacognitive therapy was found to be superior to supportive psychotherapy in ameliorating ADHD symptoms. Clinicians should consider various attention-focusing interventions for ADHD patients with insufficient response to medication. We now have several promising leads. To disseminate these approaches, researchers might develop computer-based interventions that engage, sustain, and train the ADHD patient's attention.

[http://psychiatry.jwatch.org/  
cgi/content/full/2010/824/1](http://psychiatry.jwatch.org/cgi/content/full/2010/824/1)

شہادت اور بہت سے وابستگانِ اقدس اہل علم اور دانشور اس جہاں سے رخصت ہو گئے تو بزم کی رونق بھی پہلے جیسی نہ رہی، لیکن اللہ کی مشیت اس مبارک کام کو مزید قوت بخشنے کی تھی۔ فروری ۱۹۷۹ء میں ایران میں شاہ پہلوی انقلابی قوتوں کے ہاتھوں ہزیمت سے دو چار ہوا اور ملک سے رافضی اراکینِ اختیار کی ایرانِ امام خمینی کی قیادت میں اسلامی انقلاب سے فیض یاب ہوا۔ پوری دنیا کے مسلمانوں کو اس انقلاب سے حوصلہ اور تیا جزیہ حاصل ہوا۔ اُمتِ مسلمہ میں گروہی اور مسلکی فرقہ بندی اور باہم تعصبات کو کم کرنے والی قوتوں کو ایک توانا سہارا مل گیا۔ ۱۹۸۸ء کی دہائی اسی عالم میں گزر گئی تا آنکہ امام خمینی کے ارشادات کی روشنی میں رہبر انقلاب ایران سید علی خامنہ ای نے ۱۹۹۰ء میں باقاعدہ سرکاری فرمان کے ذریعے مجلسِ اقدس کے عالمی مرکز کو تہران میں قائم کرنے کا اعلان فرمایا۔ آیت اللہ سید محمد باقر الحکیم اس ادارے کے پہلے سربراہ مقرر ہوئے۔ بعد ازاں وہ نجف اشرف میں اُس وقت شہید کر دیے گئے جب وہ نماز جمعہ کی ادائیگی کے بعد مسجد سے نکل رہے تھے۔ ادارے کے پہلے سیکریٹری جنرل آلیف اللہ واعظ زادہ خراسانی مقرر ہوئے۔ ان کے استعفٰی کے بعد ۱۳۴۲ھ میں آیت اللہ محمد علی تفسیری سیکریٹری جنرل مقرر کیے گئے۔ تفسیری تا حال اپنے فرائض انجام دے رہے ہیں۔ اس وقت مجلسِ اقدس ایک ثقافتی اور ترجمانی کمپلیکس ہونے کے باوصف اقوام متحدہ کے ادارے یونیسکو سے وابستہ ہے اور بہت مختصر عرصے میں اس ادارے کے علمی کارہائے نمایاں کی ایک طویل فہرست ہے، جنہیں اس ادارے سے وابستہ علم و مشائخ نے انجام دیا ہے۔ اس ادارے نے عالمی سطح پر دوصد سے زائد بین الاقوامی کانفرنسیں منعقد کی ہیں۔ ایک انٹرنیشنل یونیورسٹی کا قیام عمل میں لایا گیا ہے۔ تعلیمی ورکشاپس، مختلف مشترک موضوعات پر پنی ایج ڈی کے مقالات کی تیاری، کتب کی نمائش، متعدد دینی تحقیقی اداروں کا قیام، انٹرنیٹ پر رائج ویب سائٹ کے علاوہ ادارے کی خبر سانسِ انجمنی کا قیام اور مستقل چھاپہ خانہ مجلس کی نمایاں خدمات ہیں۔ خالص علمی سطح پر ہونے والے کام کی بہت زیادہ تفصیل کا تو یہ موقع نہیں ہے تاہم چند ایک منصوبوں کا ذکر اہل ذوق کی دلچسپی کا

ضرور موزوں جب ہوگا:

- ۱۔ مجلسِ اقدس کی علمی و تحقیقی شاخ نے ”سلسلۃ الاحادیث المشترکہ“ کے عنوان سے ایک برسے منصوبے کا آغاز کر رکھا ہے جس کے تحت اہل سنت اور اہل تشیع کے درمیان مختلف موضوعات پر مشترک احادیث کو الگ الگ جمع کر دیا گیا ہے۔ میں سے زائد عنوانات پر علیحدہ علیحدہ کتابیں چھپ چکی ہیں۔ مزید کام جاری ہے۔ بطور نمونہ چند موضوعات درج ذیل ہیں۔
- اخلاقیات، نماز، عبادات، مآثور و غیرہ، وحدتِ اسلامی، اقتصادِ معیشت، احادیثِ قدسیہ، حدود و قصاص، کتابِ البیوع اور امام مہدی۔
- ۲۔ دوسرا منصوبہ ان راویوں کی الگ سے ترتیب و جمع بندی ہے جن سے اہل سنت اور اہل تشیع کے آئمہ محدث روایت کرتے رہے ہیں۔ ”تفسیر و تفسیر“
- ۳۔ تیسرا عظیم الشان منصوبہ بعنوان ”موسوعة اصول الفقہ المعاصر“ ہے۔ یہ ایک انسائیکلو پیڈیا ہے جس میں چھ مذاہب (حنفی، مالکی، شافعی، حنبلی، جعفری، زیدی) کے مشترک فقہی اصول اور ان سے طریقہ استنباط کا بعداً مسئلہ احاطہ کیا گیا ہے۔ اس انسائیکلو پیڈیا کی دو جلدیں طبع ہو چکی ہیں۔ اس کی ترتیب موضوعی نہیں بلکہ الف بائی ہے۔ جامع حوالہ جات اور حواشی قابلِ دید ہیں۔
- ۴۔ چوتھا قائل ذکر علمی منصوبہ جو مکمل ہو کر شائع ہو چکا ہے وہ اندلس کے مشہور فقیہ، فلسفی اور طبیب علامہ ابن رشد کی مشہور زمانہ کتاب بدایۃ المہجد پر فقہ جعفری و زیدی کا اضافہ ہے۔ یہ درجہ کہ مذکورہ کتاب ہمارے دینی مدارس میں فقہ مقارن کی معتبر کتاب جانی جاتی ہے اور باقاعدہ نصاب میں شامل ہے۔ اس تقریبی اضافے کا ایک فائدہ طلبہ کو یہ ہوا ہے کہ پوری کتاب کی تحقیق میسر آگئی ہے۔ معتد علیہ کتابوں کے حوالے سے قدر و قیمت میں بھی کئی گنا اضافہ ہو گیا ہے۔ یہ کتاب چھ جلدوں میں فہرست کی ایک جلد سمیت شائع ہو چکی ہے۔ علاوہ بریں متعدد ایسے منصوبے زیرِ تحقیق ہیں جن کا ذکر طوالت سے خالی نہیں۔

☆————☆

خلاف مجاہد الہی، محمد ططاوی اور شیخ جواد مغنیہ جیسے تحقیق نگاروں کے جواہر پارے رسالہ الاسلام کے صفحات کی زینت بنتے رہے۔ جو مضامین مجلہ میں شائع ہوتے ان میں تفسیر وحدہ یث، اصولی حدیث، فقہ و کلام، اجتہاد و قیاس، اقتصاد و معاشرت جیسے موضوعات پر انفرادیہ کے آراء کے ساتھ فقہ جعفریہ و امامیہ کی تفصیل بھی پیش کی جاتی تھیں۔ متعدد اہم مسائل پر دونوں کا دلچسپ موازنہ بھی شائع ہوتا۔ ان کوششوں کے نتیجے میں اہل علم کے درمیان شیعہ و سنت کے بارے میں تضاد اختلاف کا تاثر نہ صرف زائل ہوا بلکہ قربت و اختلاف کا نقش گہرا ہوتا چلا گیا۔

اسی زمانے میں شیخ الازہر جناب علامہ محمود عقیق نے جامعہ الازہر کے دارالافتاء سے ۱۷ ربیع الاول ۱۳۷۸ھ کو ایک فتویٰ صادر کیا جس میں واضح کر دیا کہ افراد امت جس طرح خدا ہب اربعہ پر جلاتا مل عمل پیرا ہوتے ہیں اسی طرح وہ مذہب جعفریہ و امامیہ پر بھی عمل کر سکتے ہیں۔ خدا ہب معمول بہا میں جو دنیا و آخرت کے فائدہ کو حاصل ہے وہی فقہ جعفری کا بھی ہے۔ اس تاریخی فتویٰ کو عالم اسلام میں بے پناہ شہرت اور اہل علم میں قبول عام حاصل ہوا۔ مجلس ائقریب کی جانب سے مصر کے بعد اس فتویٰ کی باقاعدہ رونمائی کا اہتمام لبنان، شام، عراق اور پھر ایران میں کیا گیا۔ ایران میں تو خود شاہ ایران نے مخصوص سیاسی حمایت و مفادات سمیٹنے کے لئے فتویٰ حاصل کرنے اور حکومتی سطح پر شائع کرنے کی بہت کوشش کی، تاہم شیخ محمد تقی اور دیگر علماء نے شاہ کو فتویٰ فراہم کرنے سے صاف انکار کر دیا اور علماء ایران کے ایک باوقار اجتماع میں اس کا اعلان کیا گیا۔ یہ اجتماع مشہور شہر میں امام رضا کے روضہ پر منعقد ہوا۔

مجلس ائقریب مصر میں قائم ہوئی تو بہت جلد اس کے اثرات عراق، شام، لبنان، یمن، ترکی، سعودی عرب اور پاکستان تک پہنچ گئے۔ دارائقریب قاہرہ اور بانی پاکستان جناب محمد علی جناح کے درمیان مراسلت بھی ہوئی۔ اس مراسلت کا ریکارڈ رسالہ الاسلام کے پہلے شمارہ ۱۹۳۹ء کے علاوہ دیگر ائقریب کے عنوان سے مصری وزارت اوقاف کی رپورٹ مطبوعہ ۱۹۹۱ء میں دیکھا جاسکتا ہے۔

مجلس ائقریب کی سرگرمیاں مصر میں جاری ہیں لیکن امام حسن البنا کی

میں علمی آسمان کے تابناک ستارے تھے۔ قاہرہ میں شیخ تقی کا چھوٹا سا گھرانہ حضرات کی فکری نشستوں کا مرکز بن گیا تھا۔ سب ہی ہم خیال اور بلند و ذوق انسان تھے۔ بالآخر مجالس کو گفت و شنید سے آگے ایک منظم انجمن کی شکل دینے کی اجتماعی خواہش آشکار ہو گئی۔ مجلس کا نام تجویز کرنے کا مرحلہ آیا تو مجلس المتعارف مجلس التعاون اور مجلس وحدت جیسے نام مختلف دوستوں نے تجویز کیے۔ لیکن اتفاق رائے اور پسندیدگی شیخ حسن البنا کے تجویز کردہ نام کو حاصل ہوئی۔ انہوں نے ”مجلس ائقریب“ کا عنوان منتخب فرمایا اور شیخ تقی کا گھرانہ دفتر اور مرکز قرار پایا۔ مجالس علمی جاری رہیں، بلند پایہ فقہی مسائل، اجتہاد و استنباط کے اصول، سماجی و عمرانی قبیضے زیر بحث آتے رہے۔ نیز یہ فیصلہ کیا گیا کہ ان مباحث کی اشاعت کے لئے ایک مجلہ کا اجرا کیا جائے جو مجلس ائقریب کا علمی ترجمان ہو۔ چنانچہ شیخ محمد مدنی صاحب کی ادارت میں ”رسالہ الاسلام“ کے نام سے پہلا شمارہ ۱۹۳۹ء بمطابق ربیع الاول ۱۳۶۸ھ میں منصفہ شہر دہلی آیا۔ اس رسالہ کے اجرا سے قبل امام حسن البنا نے اپنے روزنامہ کے صفحات مجلس ائقریب کے علمی و فقہی مباحث کے لئے وقف کر رکھے تھے۔ امام حسن البنا کی کوششوں سے ایرانیوں پر حج کے لئے عائد پابندی ختم ہوئی اور ایک طویل عرصہ کے بعد ایرانیوں کو حج بیت اللہ کی سعادت نصیب ہوئی۔ شیخ حسن البنا نہ صرف دارائقریب کو ماہانہ چندہ دیتے تھے بلکہ انہوں نے اپنے وابستگان سے تین رضا کار بھی ہر وقت مجلس ائقریب کے لیے وقف کر دیے تھے۔ امام حسن البنا نے اپنے اخبار میں مذہب جعفری سمیت دیگر فقہاء کی آرا کے مطابق مسائل حج شائع کیے انہوں انہیں حج کے موقع پر سعودی عرب روانہ کیا۔ ان مسائل حج کو پوری دنیا کے مسلمانوں میں بہت قبولیت حاصل ہوئی۔

رسالہ الاسلام ایک سہ ماہی مجلہ تھا جو اپنی تاریخ اجرا سے لے کر مسلسل ۲۳ سال رمضان ۱۳۹۲ھ بمطابق اکتوبر ۱۹۷۱ء تک بغیر کسی تعطیل کے شائع ہوتا رہا۔ اس رسالے میں مصر، عراق، شام اور ایران کی مشہور ترین علمی ہستیاں تحقیقی مضامین لکھتی رہیں۔ شیخ ابو زہرہ، غریبہ جدی، علی حدی، علامہ عبدالوہاب

## مجلس التقريب بين المذاهب الاسلاميه

تاریخی پس منظر

.....مولانا عبدالحق ہاشمی.....

جعفری یا فقہ زیدی کو مذاہب اربعہ کے مماثل اور ہم پلہ قرار دینے کا موضوع تقریباً خارج ہی رہا۔ علما و محققین کی کاوشوں کا اہمیت یہ فائدہ ضرور ہوا کہ بحیثیت مجموعی اہل تشیع ہمیشہ (اہل سنت والجماعہ) یا امیہ مسلک کا باقاعدہ حصہ رہے۔ ان پر فتویٰ ہائے کفر ہمیشہ سخت متعصب اور شدید مخالفین نے ہی لگائے لیکن انہیں معاشرے میں چنداں قبولیت حاصل نہ ہو سکی۔

ایران کے شیخ محمد تقی مکی ان منفر د لوگوں میں سے تھے جو تقریب المذہب کی علمی تحریک سے نہ صرف متاثر ہوئے بلکہ انہوں نے اس فکر کو ایک جامع اور منظم صورت میں ڈھالنے کے لئے بہت فعال اور ایثار کھٹی پریشانی کرنا یاد کیا۔ انہوں نے ایران سے ہجرت کر کے پہلے لبنان اور پھر مصر کو جائے سکونت بنایا۔

سب سے پہلے جامعہ الازہر کے شیخ محمد المراغی سے ملاقات کی اور تفصیل سے گفتگو کی۔ شیخ الازہر محمد المراغی خود بھی ایک متبحر عالم دین اور وسیع الشرب فقیہ تھے۔ دونوں کی ملاقات دو تہائی میں ڈھل گئی۔ شیخ مراغی نے شیخ محمد تقی کو ازہر شریف میں فلسفے کی سند ریس پیش کی جسے شیخ تقی نے قبول کر لیا۔ اس دوران شیخ مراغی محمد تقی کو ازہر شریف میں فلسفے کی سند ریس پیش کی جسے شیخ تقی نے قبول کر لیا۔ اس دوران شیخ مراغی کے توسط سے متعدد اہل علم و دانش سے تعارف اور رابطہ پیدا ہوا۔ ان شخصیات میں سب سے معروف اور معتبر شخصیت اخوان المسلمون کے بانی اور مؤسس امام حسن البنا تھے۔ ان کے علاوہ شیخ مصطفیٰ عبدالعزیز، شیخ عبدالحمید سلیم، شیخ محمود دھوتو اور مشہور تھیسر روح المعانی کے مصنف شیخ محمود الوسی کے فرزند سید الوسی بھی شامل تھے۔ یہ مشائخ اس وقت مصر

مجلس تقریب کے بارے میں کچھ تذکرہ فادے سے خالی نہ ہوگا۔ یہ مجلس بالکل اچانک وجود میں نہیں آئی بلکہ عرب و عجم سے تعلق رکھنے والی مختلف شخصیات کے قلب و دماغ میں برسوں اس کا خیال ایک خواب کی طرح چھایا رہا اور عرصہ طویل تک جاری رہا۔ بہت دور نہیں تو برصغیر میں شاہ ولی اللہ دہلوی کی کتب میں اس فکر کا انعکاس بہت واضح طور پر نظر آتا ہے۔ پھر علامہ محمد اقبال اور مولانا سید ابوالاعلیٰ مودودی کو ساری زندگی اسی کاوش و جہد کا عملی نمونہ نظر آتی ہے۔ ایشیائے کوچک سے لے کر سرزمین عرب تک کو اس فکر سے متاثر کرنے والی شخصیت سید جمال الدین افغانی بھی اپنے کارہائے نمایاں میں بلند مقام پر فائز نظر آتے ہیں۔ متذکرہ بالا تمام شخصیات دین اسلام اور مسلمانوں کو مردہ نظام میں بالادست اور بالاعتبار بنانے، انہیں زوال کی پستیوں سے نکال کر عروج کی بلند یوں تک پہنچانے کے لئے کوشاں رہیں، عالم اسلامی میں پائے جانے والے مختلف فقہی مسالک کے درمیان اعتدال، رواداری اور برداشت کو فروغ دینے کی سعی و جہد اور تلقین و نصیحت میں مشغول رہیں، تاہم بالعموم ان کی توجہ کا مرکز مذاہب اربعہ (حنفیہ، مالکیہ، شافعیہ، حنبلیہ) کے نزاعات تک اغلباً محدود رہا یا بالخصوص برصغیر میں احناف کی نئی تقسیم (دیوبندی، بریلوی، اہل حدیث) توجہ کا ہدف رہی۔ اس طرح یہ ساری کوششیں اندرون اہل سنت ہی مرکوز رہیں۔ اہل سنت کے مقابلے میں اہل تشیع کے بارے میں عمومی معاشرتی اور سماجی دائروں کے اندر تھل اور رواکاری کا قابل قدر رویہ اور اس کی مزید ترویج کا داعیہ موجود رہا لیکن خالص علمی و فقہی اصولوں کی روشنی میں اہل تشیع کے ہاں قابل تقلید فقہ



Remarks about the bulletin

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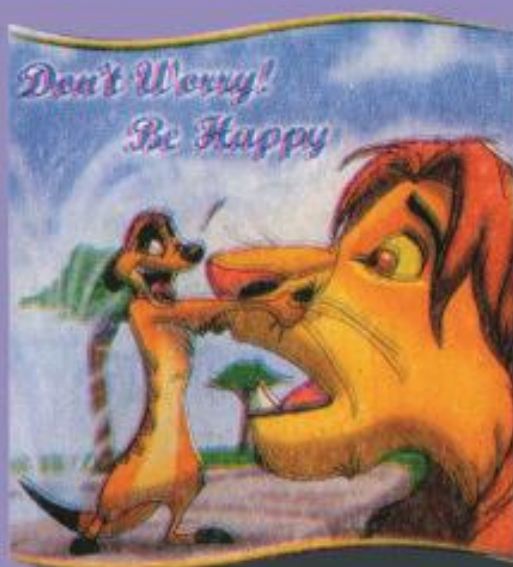
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