Anxiety Disorders

**Generalized Anxiety Disorder**

JAMA, 02/09/2011

Torpy JM et al. – Anxiety disorders affect more than 40 million adults in the United States alone, about 18% of the population. Worldwide, approximately 20% of persons who receive primary health care have anxiety disorders or depression


**Augmentative Quetiapine in Partial/Nonresponders with Generalized Anxiety Disorder: A Randomized, Placebo-Controlled Study.**

Authors: Altamura AC, Serati M, Buoli M, Dell’Osso B.

Department of Psychiatry, University of Milan, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy.

Abstract: Generalized anxiety disorder (GAD) is a chronic and disabling condition. The aim of this study was to evaluate the effectiveness of low-dose augmentative quetiapine (mean dose=50 mg/day) in patients with GAD and partial/no response to selective serotonin reuptake inhibitors (SSRIs). Twenty patients with GAD and partial/no response to SSRIs were randomized to quetiapine (n=10) or placebo (n=10) for 8 weeks, continuing their treatment with SSRIs. Analyses of variance with repeated measures on Hamilton Anxiety Rating Scale (HAM-A) and Clinical Global Impression (CGIs; severity of illness) were carried out at baseline and after 8 weeks and the number of responders/remitters was computed and compared between the groups. HAM-A scores at baseline were 15.60 (±4.48) in the placebo group and 18.50 (±6.59) in the quetiapine group, and at the end-point, HAM-A scores in the placebo group were 10.40 (±4.88) and 9.20 (±5.86) in the quetiapine group. A significant time-by-treatment effect was found on the HAM-A (F=5.19, P=0.035) and CGIs scores (F=19.60, P<0.001) in favor of the quetiapine group. The number of responders was numerically superior in the quetiapine group (60 vs. 30%) without reaching statistical significance (x²=1.82, degree of freedom=1, P=0.37, ϕ=0.30). Remitters were 40% for the quetiapine group versus 20% for the placebo group (x²=9.95, degree of freedom=1, P=0.06, ϕ=0.22). Low-dose augmentative quetiapine may be an useful treatment option for patients with GAD and partial/no response to SSRIs. The lack of double-blind conditions and the limited sample size may limit the confidence in the reported results. Larger randomized controlled trials are warranted to confirm these data.

Geriatric Psych

**Bupropion in the Treatment of Depression in Parkinsons Disease**

International Psychogeriatrics, 02/01/2011

Zaluska M et al. – A 78-year-old female with a nine-year history of depression was hospitalized due to worsening depression and symptoms associated with Parkinson's disease (PD). Her motor abilities improved on levodopa and the depression improved after a trial of bupropion, following unsuccessful treatment with other antidepressants

Dementia

**Antidepressants for Agitation and Psychosis in Dementia**

Cochrane Reviews, 02/23/2011 Clinical Article

Seitz DP et al. – The selective serotonin reuptake inhibitors (SSRIs) sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo in two studies

Mood Disorders

**Sex Differences In Adolescent Depression: Do Sex Hormones Determine Vulnerability**

Journal of Neuroendocrinology, 03/23/2011

Nannick EFG et al. – Depression is one of the most common, costly and severe psychopathologies worldwide. Its incidence however, differs significantly between the sexes and depression rates in women are twice those of men. Interestingly, this sex difference emerges during adolescence

J Clin Psychiatry, 2011 Feb 22. [Epub ahead of print]

**A Double-blind Placebo-Controlled Trial of Lamotrigine as an Antidepressant Augmentation Agent in Treatment-refractory Unipolar Depression.**

Authors: Barbee JG, Thompson TR, Jamhour NJ, Stewart JW, Conrad EJ, Reinherr FW, Thompson PM, Shelton RC.

3439 Magazine Street, New Orleans, LA 70115, USA. jgbmd@att.net

Arabpsy net e-Journal: N°27-28 – Summer & Autumn 2010

Patients treated with escalating doses of escitalopram up to 50 mg for up to 32 weeks until they achieved remission (Montgomery-Asberg Depression Rating Scale [MADRS] (less than or equal to 8) or failed to tolerate dose.

**Results**

- 42 patients (70%) completed study
- 21 patients (35%) achieved remission with 8 of 21 patients (38%) needing the 50 mg dose to achieve remission
- Median time to remission 24 weeks and median dose in remission 30 mg
- No significant safety issues identified although tolerability appeared to decline above dose of 40 mg with 26% of patients unable to tolerate 50 mg
- 12 (20%) patients had adverse events leading to discontinuation
- Most common AE were headache (35%), nausea, diarrhea and nasopharyngitis (all 25%)
- Minor mean weight gain found during study, which did not appear to be dose-related
- Half of patients who completed study chose to continue treatment with escitalopram rather than taper down dose at 32 weeks

**Mood Disorders**

* Deep brain stimulation for treatment-resistant depression: Follow-up after 3 to 6 years

Kennedy SH et al. – This report represents an extended follow-up of 20 patients with treatment-resistant depression who received DBS to the subcallosal cingulate gyrus (Brodman’s area 25). These data suggest that in the long term, DBS remains a safe and effective treatment for treatment-resistant depression. Additional trials with larger samples are needed to confirm these findings.

**Methods**

After an initial 12-month study of DBS, patients seen annually and at last follow-up visit to assess depression severity, functional outcomes, and adverse events.

**Results**

- Average response rates 1, 2, and 3 years after DBS implantation were 62.5%, 46.2%, and 75%
- At last follow-up visit (range=3–6 years), average response rate 64.3%
- Functional impairment in the areas of physical health and social functioning progressively improved up to the last follow-up visit
- No significant adverse events reported during this follow-up, although 2 patients died by suicide during depressive relapses
Bipolar Affective Disorders

**Meta-analysis of efficacy and treatment-emergent suicidality in adults by psychiatric indication and age subgroup following initiation of paroxetine therapy: a complete set of randomized placebo-controlled trials.**

**Authors:** Carpenter DJ, Fong R, Kraus JE, Davies JT, Moore C, Thase ME.

GlaxoSmithKline, King of Prussia, Pennsylvania.

**Abstract**

**Objective:** This meta-analysis of placebo-controlled paroxetine trials examines suicidality incidence in adults, focusing on disorder and age as potential risk factors. The findings are put in context with an efficacy meta-analysis of the same trial datasets.

**Data sources:** GlaxoSmithKline paroxetine clinical trial database(s).

**Study selection:** All double-blind, randomized, placebo-controlled, parallel-group studies of paroxetine therapy in adults enrolling at least 30 patients total were included in the analysis. The dataset comprised 14,911 patients from 61 trials.

**Data extraction:** Possible cases of suicidality were identified and blindly categorized by an expert panel, using methodology previously used by the US Food and Drug Administration. Incidences of suicidal behavior (preparatory act, suicide attempt, or completed suicide) and any suicidality (suicide behavior or ideation) were compared between paroxetine and placebo. Efficacy assessments were based on standard depression rating scales (eg, Hamilton Depression Rating Scale or Montgomery-Asberg Depression Rating Scale) and Clinical Global Impressions Improvement scale (CGI-I) scores.

**Results:** In the primary dataset, ie, all disorders combined, there were no significant differences between paroxetine and placebo for overall suicidality (suicidal behavior or ideation: n/n = 83/8,958 [0.93%] vs n/n = 65/5,953 [1.09%], respectively; OR = 0.9 [95% CI, 0.7-1.3]; P = .649) or for suicidal behavior specifically (n/n = 50/8,958 [0.56%] vs n/n = 40/5,953 [0.67%], respectively; OR = 1.2 [95% CI, 0.8-1.9]; P = .483). However, in patients with major depressive disorder (MDD), a greater incidence of suicidal behavior occurred in paroxetine-treated patients than in placebo-treated patients (n/n = 11/3,455 [0.32%] vs n/n = 1/1,978 [0.05%], respectively; OR = 6.7 [95% CI, 1.1-149.4]; P = .058). Across all indications, a higher incidence of suicidal behavior occurred in paroxetine-treated versus placebo-treated adults aged 18 to 24 years (n/n = 17/776 [2.19%] vs n/n = 5/542 [0.92%], respectively; OR = 2.4 [95% CI, 0.9-7.3]). In older age groups, no increase in suicidality was observed. Efficacy was demonstrated in all disorders evaluated, including MDD.

**Conclusions:** Across all disorders, overall suicidality incidence was similar between paroxetine and placebo. However, a higher frequency of suicidal behavior occurred with paroxetine in MDD, which was largely explained by the higher incidence in young adults. These data support the efficacy of paroxetine therapy; however, they also highlight the need for careful monitoring of suicidality during antidepressant therapy, particularly in younger adults.
Conclusions: Across all disorders, overall suicidality incidence was similar between paroxetine and placebo. However, a higher frequency of suicidal behavior occurred with paroxetine in MDD, which was largely explained by the higher incidence in young adults. These data support the efficacy of paroxetine therapy; however, they also highlight the need for careful monitoring of suicidality during antidepressant therapy, particularly in younger adults.

Neuro/Psych Pharmacol

* Neuropsychological changes and treatment response in severe depression

British Journal of Psychiatry, 02/03/2011 Exclusive author commentary

Douglas KM et al. – Despite significant impairment in neuropsychological functioning in the depression group, most measures failed to differentiate between treatment responders and non-responders at 10–14 days or at 6 weeks.

Richard Porter (02/09/2011) comments:

The study investigated whether neuropsychological changes (on conventional neuropsychological tasks and facial emotion-processing tasks) could represent early (10–14 days) and later (6 weeks) indicators of treatment response in in-patients with major depression. No previous published studies have examined neuropsychological changes in relation to treatment response at such an early stage of treatment. In acutely depressed patients, compared with well-matched healthy controls, performance was significantly impaired on tasks of verbal and visuospatial learning and memory, attention, executive functioning and facial emotion processing (effect sizes = 0.6-1.1). This widespread neuropsychological impairment is consistent with previous studies of depression, and the large magnitude of the impairment is likely to be due to the severity of depression in the current sample (MADRS score = 36).

Interestingly, whether or not depressed patients were taking antidepressant medication at the baseline assessment did not appear impact on their neuropsychological performance. During 6 weeks of treatment, only simple reaction time, verbal working memory and the recognition of angry facial expressions showed differential change in treatment responders compared with non-responders in the depression group. None of the measures showed a significant difference between treatment responders and non-responders at 10-14 days. Thus, data did not support the hypothesis that neuropsychological tasks can measure early, biological changes in patients with major depression who will go on to respond to treatment. However, particularly in the area of emotional processing, we believe that the study shows sufficient preliminary evidence of changes associated with treatment response to warrant further investigation. This may lead to a greater understanding of the neurobiology of response to treatment and the possibility of such tasks being used in clinical trials or as adjuncts to clinical assessment.

Neuropsych Sciences

Miscellaneous

* Coffee Consumption and Risk of Stroke in Women

Larsson SC et al. – After adjustment for other risk factors, coffee consumption was associated with a statistically significant lower risk of total stroke, cerebral infarction, and subarachnoid hemorrhage but not intracerebral hemorrhage. The association between coffee consumption and cerebral infarction was not modified by smoking status, body mass index, history of diabetes or hypertension, or alcohol consumption. These findings suggest that low or no coffee consumption is associated with an increased risk of stroke in women.

Substance Abuse

* Predictors for the Efficacy of Naltrexone Treatment in Alcohol Dependence: Sweet Preference

Alcohol and Alcoholism, 02/03/2011

Laaksonen E et al. – Sweet preference has a strong correlation to treatment outcomes with naltrexone, and sweet preference might be used as a predictor for better treatment results in alcoholics. The study offers one possible new explanation of the clinical observation that naltrexone is not effective for every patient.

Substance Abuse

* Treatment of Alcohol Dependence with Low-Dose Topiramate: An Open-Label Controlled Study

BMC Psychiatry, 03/16/2011 Clinical Article

Paparrigopoulos T et al. – Low-dose topiramate as an adjunct to psychotherapeutic treatment is well tolerated and effective in reducing alcohol craving, as well as symptoms of depression and anxiety, present during the early phase of alcohol withdrawal. Furthermore, topiramate considerably helps to abstain from drinking during the first 16-week post-detoxification period.

Methods:

Following a 7-10 day inpatient alcohol detoxification protocol, 90 patients were assigned to receive either topiramate (up to 75 mg per day) in addition to psychotherapeutic treatment (n=30) or psychotherapy alone (n=60).

Symptoms of depression and anxiety, as well as craving, monitored for 4-6 weeks immediately following detoxification on an inpatient basis.

Both groups followed as outpatients at weekly basis for another 4 months in order to monitor their course and abstinence from alcohol.

Results:

Marked improvement in depressive, anxiety, and obsessive-compulsive drinking symptoms observed over consecutive assessments in both study groups.

Individuals on topiramate fared better than controls (p<0.01) during inpatient treatment.

During 4-month follow up period, relapse rate lower among patients who received topiramate (66.7%) compared to those who received no adjunctive treatment (85.5%).

Time to relapse in topiramate augmentation group significantly longer compared to control group.
Median duration of abstinence 4 weeks for non-medicated group whereas it reached 10 weeks for topiramate group

No serious SE of topiramate recorded throughout study


Imaging Dopamine Transmission in Cocaine Dependence: Link Between Neurochemistry and Response to Treatment.


Department of Psychiatry and the Department of Radiology, Columbia University College of Physicians and Surgeons, New York.

Abstract

Objective: Previous research has shown that dopamine signaling in the limbic striatum is crucial for selecting adaptive, motivated behavior and that disrupted dopamine transmission is associated with impulsive and maladaptive behavior. In humans, positron emission tomography (PET) imaging studies have shown that cocaine dependence is associated with the dysregulation of striatal dopamine signaling, which is linked to cocaine-seeking behavior. The goal of the present study was to investigate whether this association applies to the treatment setting. The authors hypothesized that dopamine signaling in the limbic striatum would be associated with response to a behavioral treatment that uses positive reinforcement to replace impulsive cocaine use with constructive personal goals. Method: Prior to treatment, cocaine-dependent subjects underwent two PET scans using [(11)C]raclopride, before and after the administration of a stimulant (methylphenidate), for measurement of striatal dopamine D(2/3) receptor binding and presynaptic dopamine release. Results: Both of the outcome measures were lower in the volunteers who did not respond to treatment than in those who experienced a positive treatment response. Conclusions: These findings provide insight into the neurochemistry of treatment response and show that low dopamine transmission is associated with treatment failure. In addition, these data suggest that the combination of behavioral treatment with methods that increase striatal dopamine signaling might serve as a therapeutic strategy for cocaine dependence.

Anxiety Disorders

Treatment-seeking for social anxiety disorder in a general outpatient psychiatry setting

Psychiatry Research, 04/29/2011

Dalrymple KL et al. – A regression analysis found that depressive disorder not otherwise specified (DDNOS) was the most robust predictor of treatment-seeking for social anxiety disorder (SAD) status, followed by the number of feared social situations. Other factors should be examined in the future, such as knowledge of SAD and available treatment options.

Child & Adolescent Psy

Anxiety symptoms among adolescents in Japan and England; their relationship with self-construal and social support

Depression and Anxiety, 04/29/2011

Essau CA et al. – Adolescents in England reported significantly higher levels of anxiety symptoms than adolescents in Japan. In both countries, independent self-construal was negatively associated with anxiety symptoms, while interdependent self-construal was positively associated with anxiety. Path analysis showed that the effect of interdependent self-construal seemed to be weaker in Japan than in England.

The parallel development of ODD and CD symptoms from early childhood to adolescence

European Child and Adolescent Psychiatry, 04/29/2011 Clinical Article

Diamantopoulou S et al. – This study examined the developmental relations between symptoms of oppositional defiant disorder (ODD) and conduct disorder (CD) from early childhood to adolescence. The authors conclude that without the initial presence of CD symptoms, ODD symptoms are not developmental precursors to CD symptoms.

Methods

• Tested, according to parent-reported problems, whether symptoms of ODD precede development of CD symptoms, whether ODD and CD symptoms are reciprocally associated across time, or whether ODD and CD symptoms develop parallel to each other across time

• Participants were community–based sample (at time 1: N = 485, 48% boys) assessed biannually 5 times from age 4 to 6 until age 12–14

Results

• Control for stability effects, baseline SES, and symptoms of attention deficit hyperactivity disorder, ODD and CD symptoms develop parallel to each other

• No gender differences obtained

Eating Disorders

Olanzapine versus placebo for out-patients with anorexia nervosa.

Attia E, Kaplan AS, Walsh BT, Gershkovich M, Yilmaz M, Musante D, Wang Y.

Columbia University College of Physicians and Surgeons, New York, NY, USA.
Abstract

Background: Anorexia nervosa (AN) is a serious psychiatric illness associated with significant morbidity and mortality. There is little empirical support for specific treatments and new approaches are sorely needed. This two-site study aimed to determine whether olanzapine is superior to placebo in increasing body mass index (BMI) and improving psychological symptoms in out-patients with AN.

Methods: A total of 23 individuals with AN were randomly assigned in double-blind fashion to receive olanzapine or placebo for 8 weeks together with medication management sessions that emphasized compliance. Weight, other physical assessments and measures of psychopathology were collected.

Results: End-of-treatment BMI, with initial BMI as a covariate, was significantly greater in the group receiving olanzapine \( F(1, 20)=6.64, p=0.018 \). Psychological symptoms improved in both groups, but there were no statistically significant group differences. Of the 23 participants, 17 (74\%) completed the 8-week trial. Participants tolerated the medication well with sedation being the only frequent side effect and adverse metabolic effects were noted.

Conclusions: This small study suggests that olanzapine is generally well tolerated by, and may provide more benefit than placebo for out-patients with AN. Further study is indicated to determine whether olanzapine may affect psychological symptoms in addition to BMI.

Geriatric Psych

**A Systematic Review of Treatments for Refractory Depression in Older People.**

Authors: Cooper C, Katona C, Lyketsos K, Blazer D, Brodaty H, Rabins P, de Mendonça Lima CA, Livingston G.

Department of Mental Health Sciences, University College London.

Abstract

Objective: The authors systematically reviewed the management of treatment-refractory depression in older people (defined as age 55 or older). Method: The authors conducted an electronic database search and reviewed the 14 articles that fit predetermined criteria. Refractory depression was defined as failure to respond to at least one course of treatment for depression during the current illness episode. The authors rated the validity of studies using a standard checklist and calculated the pooled proportion of response to any treatment reported by at least three studies. Results: All the studies that met inclusion criteria investigated pharmacological treatment. Most were open-label studies, and the authors found no double-blind randomized placebo-controlled trials. The overall response rate for all active treatments investigated was 52\% (95\% CI=42-62; N=381). Only lithium augmentation was assessed in more than two trials, and the response rate was 42\% (95\% CI=21-65; N=57). Only two studies included comparison groups receiving no additional treatment, and none of the participants in these groups responded. In single randomized studies, extended-release venlafaxine was more efficacious than paroxetine, lithium augmentation more than phenelzine, and selegiline more than placebo. Conclusions: Half of the participants responded to pharmacological treatments, indicating the importance of managing treatment-refractory depression actively in older people. The only treatment for which there was replicated evidence was lithium augmentation. Double-blind randomized controlled trials for management of treatment-refractory depression in older people, encompassing pharmacological and nonpharmacological therapies and populations that reflect the levels of physical and cognitive impairment present in the general older population with depression, are needed.

Others

- **The interactions between religion, religiosity, religious delusion/hallucination, and treatment-seeking behavior among schizophrenic patients in Taiwan**

Psychiatry Research, 04/29/2011

Huang CLC et al. – Patients with religious delusions/hallucinations did not necessarily have more severe psychopathology. There are different profiles associated with religious affiliation/religiosity and religious delusions/hallucinations in relation to treatment-seeking behavior among schizophrenic patients in Han–Chinese society.

Mood Disorders

- **Deep brain stimulation for treatment-resistant depression: Follow-up after 3 to 6 years**

American Journal of Psychiatry, 02/04/2011 Clinical Article

Kennedy SH et al. – This report represents an extended follow-up of 20 patients with treatment-resistant depression who received DBS to the subcallosal cingulate gyrus (Brodman's area 25). These data suggest that in the long term, DBS remains a safe and effective treatment for treatment-resistant depression. Additional trials with larger samples are needed to confirm these findings.

Methods

- After an initial 12-month study of DBS, patients seen annually and at last follow-up visit to assess depression severity, functional outcomes, and adverse events

Results

- Average response rates 1, 2, and 3 years after DBS implantation were 62.5\%, 46.2\%, and 75\%.
- At last follow-up visit (range=3–6 years), average response rate 64.3\%.
- Functional impairment in the areas of physical health and social functioning progressively improved up to the last follow-up visit
- No significant adverse events reported during this follow-up, although 2 patients died by suicide during depressive relapses
Mood Disorders

Efficacy, safety and tolerability of escitalopram in doses up to 50 mg in Major Depressive Disorder (MDD): an open-label, pilot study

BMC Psychiatry, 03/23/2011 Clinical Article

Wade AG et al. – Escitalopram is licensed for use at doses up to 20mg but is used clinically at higher doses. There is limited published data at higher doses and none in the treatment of MDD.

Methods

- Open-label, pilot study
- Designed to investigate efficacy, safety and tolerability of escitalopram in doses up to 50 mg in MDD
- Conducted in 60 primary care patients with MDD who had not responded to adequate treatment with citalopram
- Patients treated with escalating doses of escitalopram up to 50 mg for up to 32 weeks until they achieved remission (Montgomery-Asberg Depression Rating Scale [MADRS]) (less than or equal to 8) or failed to tolerate dose

Results

- 42 patients (70%) completed study
- 21 patients (35%) achieved remission with 8 of 21 patients (38%) needing the 50 mg dose to achieve remission
- Median time to remission 24 weeks and median dose in remission 30 mg
- No significant safety issues identified although tolerability appeared to decline above dose of 40 mg with 26% of patients unable to tolerate 50 mg
- 12 (20%) patients had adverse events leading to discontinuation
- Most common AE were headache (35%), nausea, diarrhea and nasopharyngitis (all 25%)
- Minor mean weight gain found during study, which did not appear to be dose-related
- Half of patients who completed study chose to continue treatment with escitalopram rather than taper down dose at 32 week

Mood Disorders

Psychotherapy versus second-generation antidepressants in the treatment of depression: A meta-analysis

The Journal of Nervous and Mental Disease, 03/01/2011 Clinical Article

Spielmans GI et al. – Bona fide psychotherapies showed equivalent efficacy in short-term and slightly better efficacy on depression rating scales at follow-up relative to SGA

Results

- Bona fide psychotherapies had significantly worse short-term outcomes than medication (d = 0.58)
- No significant differences emerged between treatments in terms of response or remission rates, but non-bona fide therapies had significantly lower rates of study completion than medication (OR = 0.55)

Mood Disorders

Mirtazapine augmentation for selective serotonin reuptake inhibitor-induced sexual dysfunction: A retrospective investigation.

Authors: Atmaca M, Korkmaz S, Topuz M, Mermi O.

Source: Department of Psychiatry, School of Medicine, Firat University, Elazig, Turkey.

Abstract: The aim of the present study was to retrospectively identify sexual dysfunction changes in the patients under mirtazapine-augmented serotonin reuptake inhibitor (SSRI) treatment. The study comprised medical records of 20 outpatients, under mirtazapine-augmented SSRI treatment for their major depressive disorder, who had been selected among the patients that had developed sexual dysfunction to previous treatment as monotherapy, with SSRI for at least six weeks. These drugs were maintained and mirtazapine were added (15-45 mg/day). There was a significant difference in scores between baseline and week 4 or week 8 on the both Hamilton Depression Rating and Arizona Sexual Experience Scale. According to Clinical Global Impression-Improvement, 68.4% of the patients were responders. The use of low-dose Mirtazapine as an add-on treatment to SSRIs appears to be an effective and well-tolerated augmentation for sexual dysfunction caused by SSRIs.

Bipolar Affective Disorders

BAD

Neuropsychopharmacology, 2011 Apr 27. [Epub ahead of print]

Dopamine Transporter Gene Variant Affecting Expression in Human Brain is Associated with Bipolar Disorder.

Authors: Pinsonneault JK, Han DD, Burdick KE, Katak M, Bertolino A, Malhotra AK, Gu HH, Sadee W.

Source: Department of Pharmacology and Program in Pharmacogenomics, The Ohio State University, Columbus, OH, USA.

**Abstract:** The gene encoding the dopamine transporter (DAT) has been implicated in CNS disorders, but the responsible polymorphisms remain uncertain. To search for regulatory polymorphisms, we measured allelic DAT mRNA expression in substantia nigra of human autopsy brain tissues, using two marker SNPs (rs6347 in exon 9 and rs27072 in the 3'UTR). Allelic mRNA expression imbalance (AEI), an indicator of cis-acting regulatory polymorphisms, was observed in all tissues heterozygous for either of the two marker SNPs. SNP scanning of the DAT locus with AEI ratios as the phenotype, followed by in vitro molecular genetics studies, demonstrated that rs27072 C>T affects mRNA expression and translation. Expression of the minor T allele was dynamically regulated in transfected cell cultures, possibly involving microRNA interactions. Both rs6347 and rs3836790 (intron8 5/6 VNTR) also seemed to affect DAT expression, but not the commonly tested 9/10 VNTR in the 3'UTR (rs28363170). All four polymorphisms (rs6347, intron8 5/6 VNTR, rs27072 and 3'UTR 9/10 VNTR) were genotyped in clinical cohorts, representing schizophrenia, bipolar disorder, depression, and controls. Only rs27072 was significantly associated with bipolar disorder (OR=2.1, p=0.03). This result was replicated in a second bipolar/control population (OR=1.65, p=0.01), supporting a critical role for DAT regulation in bipolar disorder. Neurropsychopharmacology advance online publication, 27 April 2011; doi:10.1038/npp.2011.45.

**Results**

- Relative to healthy comparison subjects, both patient groups showed significantly reduced connectivity in prefrontal-limbic-thalamic areas bilaterally.
- Nonrefractory group showed more distributed decrease in connectivity than refractory group, especially in anterior cingulate cortex and in amygdala, hippocampus, and insula bilaterally.
- Refractory group showed disrupted functional connectivity mainly in prefrontal areas and in thalamic areas bilaterally.

**Sexual Disorders**

**Miscellaneous**

- **Improvement in sexual functioning in patients with type 2 diabetes and depression treated with bupropion.**
  
  Sayuk GS, Gott BM, Nix BD, Lustman PJ.

  **Source:** Department of Psychiatry, Washington University School of Medicine, St Louis, Missouri, USA.

  **Abstract**

  **Objective:** Major depressive disorder (MDD) and type 2 diabetes have independent adverse effects on sexual functioning (SF). Bupropion (BU) reportedly has few sexual side effects, but its use in diabetes has not been studied.

  **Research design and methods:** This article reports a planned secondary analysis of SF in 90 patients with type 2 diabetes treated with BU for MDD.

  **Results:** At baseline, 71.1% of patients had insufficient SF. Mean Sexual Energy Scale (SES) scores improved during treatment (P < 0.0001), as did the percentage with sufficient SF (30.6 vs. 68.1%, P = 0.001). Patients with persistent hyperglycemia had higher rates of sexual dysfunction; however, SES improvement was evident in some with persistent depression or hyperglycemia (18.2% and 25.9%, respectively).

  **Conclusions:** Insufficient SF is prevalent and may be suspected in patients with MDD and type 2 diabetes. BU treatment of MDD had few sexual side effects and was associated with significant improvements in SF.

**Schizophrenia/Psychosis**

**SChiz**

- **Deep transcranial magnetic stimulation add-on for treatment of negative symptoms and cognitive deficits of schizophrenia: a feasibility study.**

  **Authors:** Levkovitz Y, Rabany L, Harel EV, Zangen A.

  **Source:** The Emotion-Cognition Research Center, Shalvata Mental Health Care Center, Hod-Hasharon, Israel, affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.
Abstract: Treatment for negative symptoms and cognitive deficits, core elements of schizophrenia, remains inadequate. Stimulation of the prefrontal cortex via transcranial magnetic stimulation (TMS) yields only moderate results, possibly due to limited stimulation depth. Deep-TMS enables deeper and wider stimulation than before. This preliminary study is the first to examine deep-TMS as a possible add-on treatment for negative symptoms and cognitive deficits of schizophrenia. The effect of 20 daily deep-TMS sessions (20 Hz, 120% motor threshold) over the prefrontal cortex of 15 patients indicated improvement in cognition and negative symptoms that was maintained at 2-wk post-treatment follow-up.