

Psychiatry Research Review™

Making Education Easy

Issue 14 – 2009

In this issue:

- *Psychotic symptoms: narcolepsy vs schizophrenia*
- *SSRIs, pregnancy and gestational hypertension*
- *Interpersonal psychotherapy for perinatal depression*
- *No to antidepressants in bipolar disorder?*
- *Add-on lamotrigine useful in bipolar depression*
- *fMRI uncovers the psychopathy construct?*
- *Causes of clozapine discontinuation*
- *Brief CBT has potential in schizophrenia*
- *Group psychoeducation for bipolar disorders*
- *Placebo response in adolescent depression*

Welcome to the fourteenth issue of Psychiatry Research Review.

Among the studies covered in this edition, two consider aspects of antidepressant treatment during pregnancy; brief interpersonal psychotherapy may prove to be an effective and popular alternative to medication. Similarly, there were beneficial effects on relapse and rehospitalisation following brief cognitive behavioural therapy provided by mental health nurses for community-based patients with schizophrenia, and 6-month group psychoeducation had long-lasting prophylactic effects in bipolar disorder. We also discuss findings showing no long-term harm from use of placebo in adolescent depression; delaying active therapy did not impair long-term outcomes.

I hope you enjoy this edition and I welcome your comments and feedback.

Kind regards,

Dr Chris Tofield

Medical Advisor, Research Review

christofield@researchreview.co.nz

Psychotic symptoms in narcolepsy: phenomenology and a comparison with schizophrenia

Authors: Fortuyn HA et al

Summary: Psychotic symptoms were compared between 60 patients with narcolepsy, 102 with schizophrenia and 120 matched healthy controls. The researchers also compared the prevalence of formal psychotic disorders between narcolepsy patients and controls. Narcoleptics reported multisensory “holistic” hallucinations, differing from the predominantly verbal-auditory sensory hallucinations of schizophrenia. Psychotic symptoms such as delusions were not more frequent in narcolepsy compared to population controls. In addition, the prevalence of formal psychotic disorders was not increased in patients with narcolepsy. Almost half of narcoleptics reported that hypnagogic hallucinations interfered with functioning, mostly due to related anxiety.

Comment: An interesting, if difficult to read, exploration of the phenomenological gulf between narcolepsy and schizophreniform psychosis. Given the doubtful frequency of genuine ‘diagnostic dilemmas’ in this regard, the work is of more theoretical than practical interest.

Reference: *Gen Hosp Psychiatry. 2009;31(2):146-54*

[http://www.ghpjournal.com/article/S0163-8343\(08\)00241-7/abstract](http://www.ghpjournal.com/article/S0163-8343(08)00241-7/abstract)

COMING SOON to South Africa

SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

Selective serotonin reuptake inhibitor use and risk of gestational hypertension

Authors: Toh S et al

Summary: To investigate the effects of selective serotonin reuptake inhibitors (SSRIs) on the risks of gestational hypertension and pre-eclampsia, data were examined from 5731 women with nonmalformed infants and without pregestational hypertension who participated in the Slone Epidemiology Center Birth Defects Study from 1998 to 2007. SSRI treatment 2 months before pregnancy was associated with an increased risk for gestational hypertension (with or without pre-eclampsia), especially among women who continued their SSRI exposure. Gestational hypertension occurred in 9% of the 5532 women who were not treated with SSRIs and 19.1% of the 199 women who were treated with SSRIs. Among women who received treatment, gestational hypertension occurred in 13.1% of the 107 women who discontinued their SSRI by the end of the first trimester and in 26.1% of the 92 women who continued treatment beyond the first trimester. Pre-eclampsia developed in 2.4% of the women who were not treated with SSRIs, 3.7% of the women who were exposed to SSRIs only in the first trimester, and 15.2% of women who continued their SSRI treatment beyond the first trimester.

Comment: A fascinating, if incomplete, report of SSRI antidepressant effects in pregnancy. Despite multiple problems in methodology (for example, the authors did not conduct a medical record review and thus relied completely on self-report with all attendant biases), the results indicate an important association between continuing SSRI treatment and possible pre-eclampsia. Whether causal or not, the finding deserves to be further explored and considered by clinicians and patients alike. Further exploration of the clinical implications (and possible basic mechanisms) of the finding are available in an accompanying editorial (Am J Psychiatry 166:268-270, March 2009). The role of psychosocial therapies is particularly relevant; these need to be available as alternatives before, during, and after pregnancy.

Reference: Am J Psychiatry. 2009;166:320-8

<http://ajp.psychiatryonline.org/cgi/content/abstract/166/3/320>

A randomized controlled trial of culturally relevant, brief interpersonal psychotherapy for perinatal depression

Authors: Grote NK et al

Summary: The usefulness of culturally relevant, brief interpersonal psychotherapy (IPT-B) was compared with enhanced usual care for the treatment of antenatal depression in 53 low-income, pregnant women attending an urban obstetrics and gynaecology clinic. They were randomised to receive either enhanced IPT-B (an engagement session followed by 8 acute IPT-B sessions before the birth and maintenance IPT up to 6 months postpartum) or enhanced usual care, both of which were delivered in the clinic. According to intent-to-treat analyses, compared with enhanced usual care, enhanced IPT-B significantly ameliorated depression diagnoses and depressive symptoms before childbirth (3 months post-baseline) and at 6 months postpartum and improved social functioning at 6 months postpartum.

Comment: As indicated in the article above, antidepressants are a concern and can be problematic in pregnancy. Accordingly, this finding of the usefulness of IPT in pregnancy is timely. It will be important to consider the 'cultural sensitivity' of any such intervention, and particularly how it would wash with Māori in NZ.

Reference: Psychiatr Serv. 2009;60:313-21.

<http://psychservices.psychiatryonline.org/cgi/content/abstract/60/3/313>

Psychiatry Research Review and its advising experts operate independently of support sponsors. Advertising revenue supports the organisation's activities and enables the production of the regular reviews. Sponsor companies have no influence or involvement in selection and creation of content/editorial and do not view final content before it is distributed.

Correlates of treatment-emergent mania associated with antidepressant treatment in bipolar depression

Authors: Frye MA et al

Summary: This study presents outcomes for 176 adult outpatients with bipolar disorder in a 10-week trial comparing bupropion, sertraline, and venlafaxine as adjunctive antidepressant treatment for depression. After 10 weeks, 85 patients had responded to antidepressant treatment based on Clinical Global Impression Scale for Bipolar Disorder scores; 45 did not respond and 46 had treatment-emergent mania or hypomania. Depressed patients who rapidly switched to mania had significantly more severe manic symptoms at baseline as measured by the Young Mania Rating Scale (mean 3.7 vs 1.8 for responders and 2.3 for nonresponders). Patients with treatment-emergent mania also had higher scores on the Clinical Global Impression scale modified for use in bipolar disorder (mean 1.5 vs 1.1 and 1.2, respectively). Individual symptoms that predicted treatment-emergent mania were increased motor activity, speech, and thought content disorder.

Comment: The intriguing and challenging coincidence of depressive and manic symptoms has been recognised for over a century. This study explores an important facet of this problem for clinicians, and deserves to be read especially by psychiatrists working in acute inpatient settings, as it has direct management implications. The results are usefully complemented by an editorial in the same journal (Am J Psychiatry. 2009;166:127-30).

Reference: Am J Psychiatry. 2009;166:164-72

<http://tinyurl.com/c825lj>

Subscribing to Research Review

To subscribe or download previous editions of Research Review publications go to www.researchreview.co.za

COMING SOON to South Africa

SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

Psychopathic traits and deception: functional magnetic resonance imaging study

Authors: Fullam RS et al

Summary: Psychopathic traits were assessed using the Psychopathic Personality Inventory (PPI) in 24 male volunteers who conducted a simple deception paradigm while undergoing functional magnetic resonance imaging. Mean response times were greater for the lie than truth condition. Lie responses resulted in enhanced activation of the ventrolateral prefrontal cortex. The PPI sub-scales, coldheartedness, fearlessness, Machiavellian egocentricity, social potency and stress immunity correlated with activation patterns in the brain circuitry implicated in both deception and related processes such as behavioural restraint and social cognition.

Comment: Despite its small sample size, this innovative study sheds light on a key element of psychopathy: the capacity to willfully deceive. One would ordinarily insist on extension to a forensic population, but this may not be necessary since the volunteers were all Australian. In all seriousness, the finding deserves to be replicated in clinical samples; a within-subject comparison of mood states (for example bipolars at different stages of illness) would also be of interest.

Reference: *Br J Psychiatry.* 2009;194(3):229-35

<http://bjp.rcpsych.org/cgi/content/abstract/194/3/229>

*Independent commentary
by Associate Professor David
Menkes, Waikato Clinical School,
University of Auckland.*

Efficacy and safety of lamotrigine as add-on treatment to lithium in bipolar depression: a multicenter, double-blind, placebo-controlled trial

Authors: van der Loos ML et al

Summary: The efficacy and safety of lamotrigine as add-on treatment to lithium was investigated in the acute treatment of bipolar depression. 124 outpatients aged ≥ 18 years with a DSM-IV bipolar I or II disorder and a major depressive episode while receiving lithium treatment (0.6–1.2 mmol/L) were randomly assigned to 8 weeks of lamotrigine (titrated to 200 mg/day) or placebo. At week 8, the mean change from baseline in Montgomery-Asberg Depression Rating Scale (MADRS) total score was -15.38 points for lamotrigine and -11.03 points for placebo ($p=0.024$). Significantly more lamotrigine than placebo recipients were classified as responders according to the MADRS definition (51.6% vs 31.7%; $p=0.030$), but not according to the Clinical Global Impressions-Bipolar Version change of depression (64.1% vs 49.2%; $p=0.105$). Switch to mania or hypomania occurred in 5 patients (7.8%) receiving lamotrigine and 2 patients (3.3%) receiving placebo ($p=0.441$).

Comment: Lamotrigine works in bipolar depression. No doubt about it. This study provides a useful example that polypharmacy, long the norm in practice, can often be justified by controlled evidence in bipolar disorder. A specific mood-elevating effect of lamotrigine is hinted at by the slight excess of emergent mania in that group.

Reference: *J Clin Psychiatry.* 2009;70(2):223-31

<http://www.psychiatrist.com/abstracts/abstracts.asp?abstract=200902/020910.htm>

Reasons for discontinuing clozapine: matched, case-control comparison with risperidone long-acting injection

Authors: Taylor DM et al

Summary: Reasons for discontinuing clozapine were compared with those for discontinuing risperidone long-acting injection in an age-matched control group treated in the same clinical environment (161 discontinuers from each group). Adverse effects (OR, 2.19) and death (OR, 7.0) were more commonly observed as reasons for discontinuation of clozapine than of risperidone. Clozapine was less likely to be withdrawn because of ineffectiveness than was risperidone (OR, 0.034). Clozapine was associated with a significantly increased risk of death compared with that for the general population (standardised mortality ratio, 4.17). Pneumonia was the most common single cause of death.

Comment: An important and sobering reminder of the non-financial costs associated with our most effective antipsychotic.

Reference: *Br J Psychiatry.* 2009;194(2):165-7

<http://bjp.rcpsych.org/cgi/content/abstract/194/2/165>

COMING SOON to South Africa

SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

Effectiveness of brief cognitive-behavioral therapy for schizophrenia delivered by mental health nurses: relapse and recovery at 24 months

Authors: Malik N et al

Summary: The effects of brief cognitive behavioural therapy (CBT) provided by mental health nurses to community-based patients with schizophrenia were compared to treatment as usual (TAU). At 24 months' follow-up, 64 of the 205 patients (31.2%) in the CBT group had relapsed, versus 57 of 125 patients (45.6%) in the TAU group ($p=0.02$). Patients rehospitalised from the CBT group spent a total of 6710 days in hospital (mean 32.7 days), whereas rehospitalised patients from the TAU group were inpatients for 6114 days (mean 48.9 days) ($p<0.05$). Occupational recovery was achieved by 21 patients (10.2%) in the CBT group and by 17 (13.6%) in the TAU group. Mean time to relapse was 356.8 days for the CBT group and 296.1 days for the TAU group (OR, 1.592; $p=0.033$).

Comment: An intriguing UK report, not very easy to read, with potential implications for NZ community mental health teams. An economic analysis, in terms of use of inpatient services, may help to justify needed staffing expansion, should such practice be implemented here. Another interesting feature is that this work was funded by Pfizer, and most of the authors are heavily involved with various pharmaceutical companies. It remains to be clarified what is going on here.

Reference: *J Clin Psychiatry*. 2009;70(2):201-7
<http://tinyurl.com/catvf2>

Group psychoeducation for stabilised bipolar disorders: 5-year outcome of a randomised clinical trial

Authors: Colom F et al

Summary: These researchers compared the efficacy of 6-month group psychoeducation with that of non-structured group intervention on preventing recurrences and reducing time spent ill in 120 patients with bipolar disorders. At 5 years' follow-up, data were evaluable from 99 patients. Compared with non-structured group intervention, group psychoeducation was associated with prolonged time to any recurrence (log rank=9.953, $p<0.002$), fewer recurrences (3.86 vs 8.37; $p<0.0001$) of any type, fewer days with acute illness (154 vs 586 days; $p=0.0001$), and shorter length of hospitalisation per hospitalised participant (30 vs 45 days; $p=0.047$).

Comment: Another important demonstration of the role of psychosocial interventions in severe and enduring mental illness. As with the study of CBT in schizophrenia (reviewed above), the resource implications for NZ practice are important to reckon with, but can probably be justified with cost-offset arguments.

Reference: *Br J Psychiatry*. 2009;194(3):260-5
<http://bjp.rcpsych.org/cgi/content/abstract/194/3/260>

Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Privacy Policy: Research Review will record your email details on a secure database and will not release it to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

Assessment of safety and long-term outcomes of initial treatment with placebo in TADS

Authors: Kennard B et al

Summary: These researchers sought to determine whether initial assignment to receive placebo for 12 weeks followed by open active treatment as clinically indicated was associated with different levels of benefit and risk of harm across 36 weeks as compared with initial assignment to receive active treatments, using data from 439 adolescents with major depressive disorder who were randomised to receive an initial 12 weeks of treatment with fluoxetine, cognitive behavioural therapy (CBT), combination treatment with fluoxetine and CBT, or placebo. Those assigned to placebo received open active treatment as clinically indicated after 12 weeks of placebo. At week 36, response rates were 82% for the placebo/open group and 83% in the active treatment groups. Remission rates were 48% in the placebo/open group and 59% in the active treatment groups, a difference that approached statistical significance. Patients who responded to placebo generally retained their response. Those who did not respond to placebo subsequently responded to active treatment at the same rate as those initially assigned to active treatments. There were no differences between groups in rates of suicidal events, study retention, or symptom worsening.

Comment: The controversial TADS trial, despite a flawed design, continues to produce material of interest. This report usefully examines the effect of placebo and identifies a virtually identical response rate, compared with 3 'active treatments'. A serious interpretive problem remains, however, since CBT was never paired with placebo – this means that the effect of fluoxetine v CBT was never able to be fairly assessed. On the other hand, the current report provides moderately strong support (based on an impressive n) for the view that antidepressants are best reserved for cases of adolescent depression that do not respond to psychosocial intervention.

Reference: *Am J Psychiatry*. 2009;166:337-44
<http://ajp.psychiatryonline.org/cgi/content/abstract/166/3/337>

Subscribing to Research Review

To subscribe or download previous editions of Research Review publications go to www.researchreview.co.za

COMING SOON to South Africa

SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.