



Smoking during pregnancy may be associated with an increased risk of bipolar disease

News & Views

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Journal Watch

A study recently published in the *American Journal of Psychiatry* suggests that there is an association between smoking during pregnancy and increased risk of developing bipolar disorder in adult children. The study aimed to, for the first time, assess the relationship between maternal smoking and bipolar disorder in offspring, which includes 'externalizing' symptoms among its many manifestations. Discussing the study, the authors commented "much of the psychopathology associated with prenatal tobacco exposure clusters around the externalizing spectrum, which includes ADHD, oppositional defiant disorder, conduct disorder and substance abuse disorders. Although not diagnostically classified along the externalizing spectrum, bipolar disorder shares a number of clinical characteristics with these disorders, including inattention, irritability, loss of self-control, and proclivity to drug/alcohol use."

The authors examined whether offspring exposed to maternal smoking *in utero* have an increased lifetime risk of bipolar disorder after accounting for other factors related to maternal smoking. In the study, participants with bipolar disorder were ascertained from the birth cohort of the Child Health and Development Study. The authors identified case subjects by using a combination of clinical, database and direct mailing sources. All case subjects were directly interviewed and diagnosed using DSM-IV criteria. Comparison subjects were matched to case subjects on date of birth (± 30 days), sex, membership in the cohort at the time of illness onset and availability of maternal

archived sera. After adjusting for potential confounders, the authors reported that offspring exposed to *in utero* maternal smoking exhibited a twofold greater risk for bipolar disorder (overall response = 2.014; 95% CI: 1.48–2.53; $p = 0.01$). The associations were noted primarily among bipolar offspring without psychotic features.

The authors concluded that prenatal tobacco exposure may be one suspected cause of bipolar disorder. However, they pointed out that it will be necessary to account for other unmeasured familial factors before causal teratogenic effects can be suggested.

Discussing the results, Alan Brown (New York State Psychiatric Institute, NY, USA) commented, "these findings underscore the value of ongoing public health education on the potentially debilitating, and largely preventable, consequences that smoking may have on children over time."

Sources: Talati A, Bao Y, Kaufman J, Shen L, Schaefer C, Brown A. Maternal smoking during pregnancy and bipolar disorder in offspring. *Am J Psychiatry* 170(10), 1178–1185 (2013); Columbia University. New study suggests that smoking during pregnancy may increase risk of bipolar disorder in offspring. Press release: www.cumc.columbia.edu/pi/news/new-study-suggests-smoking-during-pregnancy-may-increase-risk-bipolar-disorder-offspring



Future
Medicine part of fsg

Study suggests psychophysiologic reactivity to trauma-related cues is the greatest predictor of post-traumatic stress disorder

Researchers from Boston University's School of Medicine (MA, USA), the National Center for post-traumatic stress disorder (DC, USA), VA Boston Healthcare System (MA, USA), Suffolk University (MA, USA), Massachusetts General Hospital (MA, USA) and Harvard University (MA, USA) have published results that suggest that psychophysiologic reactivity to trauma-related, script-driven imagery procedures is a promising biological predictor of a post-traumatic stress disorder (PTSD) diagnosis.

In the USA, approximately 7–12% of the general adult population suffers with PTSD. Typical sufferers of PTSD include military personnel who have faced combat, victims of sexual assault, people from conflict-ridden areas of the world and patients who have survived intensive care unit admissions.

In the study the team analyzed data from five prior studies with 150 study participants: 78 diagnosed with PTSD and 72 who had experienced trauma but did not develop PTSD. Four main predictor classes were assessed, including the measurement of psychophysiologic reactivity to trauma-related scripts; psychophysiologic reactivity to other stressful but non-trauma-related scripts; self-reported distress in response to trauma-related scripts; and self-reported distress to other stressful but non-trauma-related scripts. Psychophysiologic reactivity to trauma-related cues appeared to be the most robust predictor of PTSD.

These findings, according to the researchers, could have significant implications for the field of psychiatry. One of the study's authors Suzanne Pineles (Boston University School of Medicine) explained, "psychophysiologic reactivity to script-driven imagery is a potential experimental paradigm that could be used to index an individual's fear response," adding that "future research may extend the use of this paradigm to

other populations. For example, it is possible that individuals with other fear-based disorders, such as phobias or panic disorder, would exhibit similar patterns of reactivity to scripts describing their fear."

Source: Boston University School of Medicine. Trauma-related psychophysiologic reactivity identified as best predictor of PTSD diagnosis. Press release: www.bumc.bu.edu/2013/10/10/trauma-related-psychophysiologic-reactivity-identified-as-best-predictor-of-ptsd-diagnosis

Potential risk factors for switch from unipolar to bipolar major depressive disorder in youth with ADHD

Findings from a recent study by researchers at Harvard University (MA, USA) suggest that the team have identified sub-threshold forms of bipolar (BP)-I disorder and deficits in emotional regulation as risk factors for bipolar disorder in youth.

The authors aimed to investigate whether emotional dysregulation and subthreshold forms of BP-I disorder increase the risk of BP switches in ADHD youth with nonbipolar major depressive disorder (MDD).

The researchers used data from two large controlled longitudinal family studies of boys and girls with and without ADHD. Participants were followed over an average follow-up period of 11.4 years. The team made comparisons between ADHD youth with unipolar MDD who had and had not switched to BP-I disorder at follow-up.

The findings from the study demonstrated that the rate of conversion to BP-I disorder at follow-up was higher in MDD subjects with subthreshold BP-I disorder at baseline compared with those without (57 vs 21%; overall response = 9.57; 95% CI: 1.62–56.56; $p = 0.013$) and in

MDD subjects with deficient emotional self regulation (overall response = 3.54; 95% CI: 1.08–11.60; $p = 0.037$).

Discussing the study the authors point out that the sample was largely Caucasian, reducing the amount to which the results can be generalized to minority groups. In addition, the authors highlighted that the sample of youth with selective eating disorder was small, which limited the statistical power for some analyses.

The authors concluded that switches from unipolar MDD to BP-I disorder in children with ADHD and MDD were predicted by baseline subthreshold BP-I disorder symptoms and baseline deficits in emotional regulation. They also highlighted the need for more work to assess whether these risk factors are operant outside the context of ADHD.

Source: Biederman J, Wozniak J, Tarko L *et al.* Re-examining the risk for switch from unipolar to bipolar major depressive disorder in youth with ADHD: a long term prospective longitudinal controlled study. *J. Affect. Disord.* doi:10.1016/j.jad.2013.09.036 (2013) (Epub ahead of print).

Adding medication to behavioral therapy may not improve results in patients with alcoholism and anxiety

A recent study carried out by researchers from the Boston University (MA, USA), investigating the effects of venlafaxine and cognitive-behavioral therapy (CBT) alone and combined in the treatment of comorbid alcohol use anxiety disorders, suggests that CBT is more effective in reducing heavy drinking in anxious alcoholics compared with progressive muscle relaxation therapy (PMR) and that the addition of medication to either CBT or PMR participants does not decrease alcohol consumption.

“...the study’s findings contradict the notion that lessening anxiety symptoms necessarily leads to better control of drinking behavior.”

Participants were recruited into an outpatient anxiety treatment program via radio, web and newspaper advertisements. Telephone screenings determined initial eligibility, and potential research participants were invited to the Center for Anxiety and Related Disorders at Boston University for a more extensive assessment of alcohol use and emotional symptoms.

Inclusion criteria for subject eligibility included: DSM-IV diagnosis of alcohol abuse or dependence (alcohol use disorder [AUD]) and a diagnosis of anxiety disorder (panic disorder, social phobia or generalized anxiety disorder); minimum age of 18 years; and had expressed the desire to stop drinking alcohol completely or to reduce alcohol consumption with the possible long-term goal of abstinence.

Exclusion criteria included: DSM-IV diagnosis of bipolar disorder, schizophrenia, bulimia/anorexia, dementia or other

substance dependence, with the exception of nicotine, marijuana and caffeine dependence; medical contraindication to the use of venlafaxine; currently taking anti-craving agents, antidepressant medications, or medication known to reduce anxiety or alcohol consumption; ongoing concurrent treatment for alcohol problems; currently taking medication that has significant interactions with venlafaxine; previously received venlafaxine; currently prescribed medication with known abuse potential; and having experienced severe depression or suicidal behaviors in the past 30 days. The authors aimed to compare the efficacy and safety of using venlafaxine and CBT to encourage and aid abstinence from alcohol consumption in individuals with comorbid AUDs and anxiety disorders, as compared with combined treatment with placebo and PMR, the control treatment condition.

Participants were divided into four groups; one receiving the antidepressant venlafaxine coupled with CBT, one receiving venlafaxine with PMR, and the other groups receiving a placebo coupled with either CBT or PMR. After 11 weeks the participants in the group receiving a placebo and CBT alone reported their heavy drinking had significantly decreased compared with the other groups receiving treatment.

The authors conclude that the results of the study indicate that venlafaxine is not superior to placebo in its effects on alcohol consumption or anxiety in subjects with comorbid AUD and anxiety disorders. They also suggest that CBT alone may be valuable in assisting individuals with comorbid AUD and anxiety disorders to reduce heavy

drinking. The authors note that the study’s findings contradict the notion that lessening anxiety symptoms necessarily leads to better control of drinking behavior.

The authors suggest that, while antidepressant medications may help to control anxious feelings, the ability to acknowledge and respond to such intense feelings may be one reason that CBT is effective, and hypothesize that this may be why the addition of an antidepressant to CBT did not improve outcomes.

“This study points to the importance of behavioral approaches to decrease heavy drinking through strategies to improve emotional regulation.”

Discussing the findings, study author Domenico Ciraulo (Boston University) commented, “it is vital to find better treatments, whether they are medication therapies or behavioral interventions ... This study points to the importance of behavioral approaches to decrease heavy drinking through strategies to improve emotional regulation.”

Sources: Ciraulo D, Barlow D, Gulliver S *et al*. The effects of venlafaxine and cognitive behavioral therapy alone and combined in the treatment of co-morbid alcohol use-anxiety disorders. *Behav. Res. Ther.* doi:org/10.1016/j.brat.2013.08.003 (2013) (Epub ahead of print); Boston University. Boston University researchers test effectiveness of behavioral and medication treatments for patients with alcoholism and anxiety. Press release: www.bumc.bu.edu/2013/10/07/boston-university-researchers-test-effectiveness-of-behavioral-and-medication-treatments-for-patients-with-alcoholism-and-anxiety

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Future Medicine Ltd, Unitec House, 2 Albert Place, London, N3 1QB, UK

Tel.: +44 (0)20 8371 6090; Fax: +44 (0)20 8343 2313; a.williams@futuremedicine.com

DSM-IV-TR criteria may be insufficient and too restrictive for diagnosis of bipolar disorder

An observational, single-visit survey (Bipolact) involving 390 adult patients attending primary care for major depressive episodes (MDEs; DSM-IV-TR criteria) in 201 general practice offices in France, carried out by researchers from Zurich University (Zurich, Switzerland), suggests that diagnosis is depressed in primary care patients with previous psychiatric ICD-10 bipolar disorder (BD).

The authors report that over the past 20 years, a large amount of evidence has accumulated against the overly restrictive diagnostic concepts of hypomania in DSM-IV and the DSM-IV-TR. Therefore, they decided to test DSM-IV-TR and a broader modified version (DSM-IV-TRm) for their ability to detect bipolarity in patients who had been treated for BD in psychiatric settings, and who now consulted general practitioners (GPs) for new major MDEs. Participating GPs were trained

by the Bipolact Educational Program, and were familiar with the medical care of depressive patients.

“...very few ICD-10 bipolar patients consulting French general practitioners for major depressive episodes met DSM-IV-TR criteria for bipolar diagnosis...”

The findings demonstrated that of the 390 patients with MDE, 129 (33.1%) were previously known to be bipolar patients (ICD-10 criteria). In addition, the majority of the latter bipolar patients (89.7%) had previously been treated with antidepressants. Only 9.3% of them met DSM-IV-TR criteria for BD. Conversely, 79.1% of the 129 bipolar patients met DSM-IV-TRm criteria for BD and showed strong associations with impulse control disorders

and manic/hypomanic switches during antidepressant treatment.

Discussing the study's limitations, the authors pointed out the lack of training of participating GPs, recall bias of patients and the study not being representative for untreated bipolar patients.

The team concluded that very few ICD-10 bipolar patients consulting French GPs for MDE met DSM-IV-TR criteria for bipolar diagnosis, suggesting that DSM-IV-TR criteria are insufficient and too restrictive for the diagnosis of BD. DSM-IV-TRm was more sensitive; however, 20% of bipolar patients were still undetected.

Source: Angst J, Hantouche E, Caci H, Gaillard R, Lancrenon S, Azorin JM. DSM-IV diagnosis in depressed primary care patients with previous psychiatric ICD-10 bipolar disorder. *J. Affect. Disord.* doi:10.1016/j.jad.2013.09.028 (2013) (Epub ahead of print).

Study suggests diverse pathways to violent behavior during first-episode psychosis

A recently published study, led by researchers from the University of Warwick (UK), aimed to assess whether there are subgroups of psychotic individuals that can be characterized by different developmental trajectories to violent behavior, suggests that there are diverse pathways to violent behavior during first-episode psychosis (FEP).

Although many studies have explored the correlates of violence during FEP, most have compared violent psychotic individuals with nonviolent psychotic individuals. Accumulating evidence suggests that there may be subgroups within psychosis, differing in terms of developmental

processes and proximal factors associated with violent behavior.

“...the teams recommended off the back of these findings that, in addition to tackling illness-related risks, treatments should directly address antisocial traits as a potent risk for violence during first-episode psychosis.”

In this study the authors assessed pre-morbid delinquency (pre-morbid adjustment subscale across childhood and adolescence), age at illness onset,

duration of untreated psychosis, past drug use, positive symptoms and violent behavior. They also estimated group trajectories of pre-morbid delinquency using latent class growth analysis and additionally quantified associations with violent behavior. The study included six early intervention services in five geographical locations across the UK, with violent behavior information available for 670 FEP cases with a main outcome of violent behavior at 6 or 12 months following early intervention services entry.

The authors identified four groups of pre-morbid delinquency: stable low, adolescent-onset high to moderate, stable moderate

and stable high. Performing logistic regression analysis, with stable low delinquency as the reference group, the team demonstrated that moderate (overall response: 1.97; 95% CI: 1.12–3.46) and high (overall response: 3.53; 95% CI: 1.85–6.73) pre-morbid delinquency trajectories increased the risk of violent behavior during FEP. After the researchers had controlled for confounders, path analysis demonstrated that the increased risk for violence in the moderate delinquency group was indirect

(i.e., partially mediated by positive symptoms; probit coefficient $[\beta] = 0.12$; $p = 0.002$); while stable high delinquency directly increased the risk for violence ($\beta = 0.38$; $p = 0.05$).

The authors conclude from the results of this study that there appear to be diverse pathways to violent behavior during FEP. Stable high pre-morbid delinquency from childhood onwards seemingly directly increases the risk for violent behavior, independent of psychosis-related risk factors.

Finally, the teams recommended off the back of these findings that, in addition to tackling illness-related risks, treatments should directly address antisocial traits as a potent risk for violence during FEP.

Source: Winsper C, Singh S, Marwaha S *et al.* Pathways to violent behavior during first-episode psychosis. *JAMA Psychiatry* doi:10.1001/jamapsychiatry.2013.2445 (2013) (Epub ahead of print).

– All stories written by Dominic Chamberlain