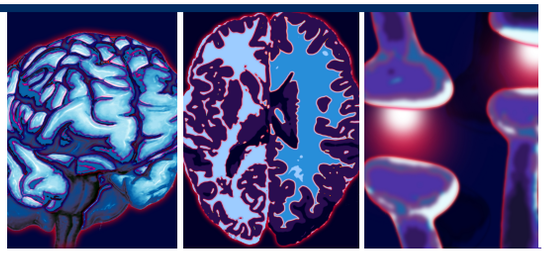

Smoking during pregnancy may be associated with increased risk of bipolar disease

A study recently published in the *American Journal of Psychiatry* suggests that there is an association between smoking during pregnancy and increased risk for developing bipolar disorder in adult children. The study aimed to, for the first time, assess in-depth the relationship between maternal smoking and bipolar disorder in offspring, which includes externalizing symptoms among its many manifestations. Discussing the study the authors wrote "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* would be at increased lifetime risk for 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 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, 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."

10.2217/NPY.13.74 © 2013 Future Medicine Ltd

– Written by Dominic Chamberlain

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, 1178–1185 (2013); Columbia University. New Study Suggests that Smoking during Pregnancy May Increase Risk of Bipolar Disorder in Offspring. Press release: http://www.cumc.columbia.edu/pi/news/new-study-suggests-smoking-during-pregnancy-may-increase-risk-bipolar-disorder-offspring

Study suggests psychophysiologic reactivity to trauma-related cues 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 nontrauma related scripts; self-reported distress in response to trauma-related scripts; and self-reported distress to other stressful but nontrauma-related scripts. Psychophysiologic reactivity to trauma-related cues appeared to be the most robust predictor of PTSD.

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These findings, according to the researchers, could have significant implications for the field of psychiatry. Suzanne Pineles (Boston University School of Medicine, MA, USA), one of the study's authors 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."

– Written by Dominic Chamberlain

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/

New potential risk factors identified 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 subthreshold forms of bipolar (BP)-I disorder and deficits in emotional regulation as risk factors for bipolar disorder in youth. In the study the authors aimed to investigate whether emotional dysregulation and subthreshold forms of BP-I disorder increase the risk for BP switches in ADHD youth with nonbipolar 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 major depression (MDD) who did and did not switch 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. Additionally 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.

– Written by Dominic Chamberlain

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:http://dx.doi.org/10.1016/j.jad.2013.09.036 (2013) (Epub ahead of print).

Study suggests that DSM-IV-TR criteria are insufficient and too restrictive for the diagnosis of bipolar disease

An observational, single-visit survey (Bipolact) involving 390 adult patients attending primary care for major depressive episodes (MDEs) (DMS-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.

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 bipolar disorders (BD) in psychiatric settings, and who now consulted general practitioners (GPs) for new major MDEs. Participating GPs (53.3 ± 6.5 years old, 80.1% male) were trained by the Bipolact Educational Program, and were familiar with the medical care of depressive patients.

The findings demonstrated that of the 390 patients with MDE, 129 (33.1%) were previously known as bipolar patients (ICD-10 criteria). Additionally, the majority of the latter bipolar patients (89.7%) had previously been treated with antidepressants. Only 9.3% of them met DMS-IV-TR criteria for BD. Conversely, 79.1% of the 129 bipolar patients met DMS-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.

– Written by Dominic Chamberlain

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.* pii: S0165-0327(13)00714-3 (2013).

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

A recently published study carried out by the National Evaluating the Development and Impact of Early Intervention Services in the West Midlands led by researchers from the University of Warwick (Warwickshire, UK) aiming to assess whether there are subgroups of psychotic individuals 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 there may be subgroups within psychosis, differing in terms of developmental processes and proximal factors associated with violent behavior.

In this study the authors assessed premorbid delinquency (premorbid adjustment adaptation 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 premorbid 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 first-episode psychosis cases with a main outcome of violent behavior at 6 or 12 months following early intervention services entry.

The authors identified four groups of premorbid 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) premorbid delinquency trajectories increased the risk for 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 [β] = 0.12; p = 0 .002); while stable high delinquency directly increased the risk for violence (β = 0.38; p = 0.05).

The authors concluded that the results suggest that there appear to be diverse pathways to violent behavior during FEP. Stable high premorbid 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.

– Written by Dominic Chamberlain

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).

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

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

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In the study 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 anticraving 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 co-morbid 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 venlaflaxine coupled with CBT, one receiving venlaflaxine 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.

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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. Additionally they suggest that CBT alone

may be valuable in assisting individuals with comorbid AUD and anxiety disorders in reducing heavy drinking. The authors point out that the findings contradict the notion that lessening anxiety symptoms necessarily leads to better control of drinking behavior.

The authors suggest, in the paper, 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 lead to improved outcomes.

Discussing the findings employed Domenico Ciraulo (Boston University, MA, USA), one of the study's authors, 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."

– Written by Dominic Chamberlain

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: http://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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