

The COMT val158met genetic variant predicts antidepressant treatment response in major depression

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Background: In this study, it was hypothesized that higher COMT activity as conferred by the COMT 158val allele leading to decreased norepinephrine and dopamine availability has a negative effect on antidepressant drug response in depression.

Methods: A sample of 322 unrelated Caucasian patients with affective disorders (DSM-IV: major depression, $n = 256$, bipolar disorder, $n = 66$) was characterized and genotyped for the COMT val158met variant. Weekly Hamilton Depression Rating Scale (HAM-D) scores during antidepressant treatment (SSRIs, NSRIs, NaSSA) were assessed. Statistical analysis was performed using stratified and adjusted multivariate ANOVA (Bonferroni post hoc test).

Results: The COMT 158val/val genotype as compared with the 158val/met genotype conferred a significant risk of worse response after 4–6 weeks of antidepressant treatment in patients with affective disorders (week 4: $P = 0.030$; week 5: $P = 0.002$; week 6: $P = 0.003$). Even more significant results were obtained for the subsample restricted to major depression (week 4: $P = 0.014$; week 5: $P = 0.000$; week 6: $P = 0.000$). Statistical comparison of COMT 158val/val vs. COMT 158met/met genotype with respect to therapy response showed a less pronounced negative effect of the COMT 158val/val genotype (week 5: $P = 0.037$; week 6: $P = 0.096$) in the sample of patients with major depression. In the subsample of patients with bipolar disorder, major depressive episode, no influence of the COMT val158met variant on HAM-D overall change scores could be detected. Further stratified results are presented.

Conclusions: In patients homozygous for the higher activity COMT 158val allele, the consecutive decreased availability of the monoamines norepinephrine and dopamine might impair the efficacy of antidepressants during pharmacological treatment in major depression.

Childhood trauma and psychosis: a critical review

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Background: A significant proportion of people with psychotic disorders report traumatic experiences in childhood, such as sexual and physical abuse. Similarly, a proportion of childhood trauma (CT) survivors report psychotic symptoms such as hallucinations and delusions. Are these psychotic symptoms in trauma survivors part of the sequelae of CT or do they occur by chance? Much of the research into the relationship between CT and psychosis has suffered from a lack of methodological rigor and thus has failed to answer this question. Past reviews have paid little attention to these methodological problems (Read 1997, 2005; Morrison 2003). The aim of this review was to synthesize and critically evaluate the evidence.

Method: Medline and Psychinfo databases were systematically searched and papers identified were assessed according to eligibility criteria. The reference sections of identified papers were also searched.

Results: Forty-nine papers were identified. The rates of CT reported in groups with psychosis ranged between 19% and 83%. Child sexual abuse prevalence rates ranged between 17% and 79%. Reports of child physical abuse ranged from 10% to 61%. When compared with nonclinical controls, those with psychosis reported more trauma. Epidemiological studies investigating the relationship of CT to psychotic diagnosis and symptoms have found mixed results. However, all studies have methodological problems.

Conclusions: These studies tentatively suggest a relationship between CT and psychosis. Further good quality research is needed to clarify any association.

The impact of age at onset of bipolar 1 disorder on functioning and clinical presentation

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Background: Recent studies have proposed the existence of three distinct subgroups of bipolar 1 based on age at onset (AAO) (Bellivier et al. 2003: *Am J Psychiatry*: 160: 999–1001; Patel et al. 2006: *Bipolar Disorders*: 8: 91–94). The present study aims to investigate potential clinical and functional differences between these subgroups.

Method: Participants ($n = 240$) were enrolled in the Bipolar Comprehensive Outcomes Study, a 2-year longitudinal observational study. Measures assessed included the Young Mania Rating Scale, Hamilton