

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

Depression Rating Scale (HAMD21), Clinical Global Impressions Scale (CGI-BP), SF-36, SLICE/Life Scale and the EuroQol. Participants were also asked about age at first major affective episode.

Results: Our data support the existence of three subgroups; early (AAO <20, mean = 15.47 ± 2.7) 46.5% of participants, intermediate (AAO 20–35, mean = 25.52 ± 4.4) 43.8% of participants and late (AAO >35, mean = 46.2 ± 10.1) 9.7% of participants. The groups differed significantly in the type of first episode experienced ($\chi^2 = 14.88$, $df = 1$, $P = 0.005$) such that the early subgroup were more likely to experience a depressive first episode, while the intermediate subgroup were more likely to experience a manic first episode. At enrollment, the early subgroup reported more severe depressive symptoms [HAM-D F(1, 153) = 10.20, $P = 0.007$]. When the early subgroup was compared with the typical subgroup (intermediate and late combined), the early subgroup tended to experience more clinically significant distress as a result of depression (CGI-BP; $\chi^2 = 3.73$, $df = 1$, $P = 0.053$), were less satisfied with their overall health (SF-36; $\chi^2 = 9.42$, $df = 4$, $P = 0.051$) and were less able to enjoy recreational activities (SLICE; $\chi^2 = 10.47$, $df = 4$, $P = 0.033$).

Conclusions: Several clinical and functional differences were found between the subgroups based on preliminary data. These differences are important as they can help guide clinical management of this debilitating disorder.

Neuropsychological function in social phobia

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Background: Studies of neuropsychological function in social phobia have focused on attentional processes, memory function, judgment and interpretation biases, but findings have been conflicting. Differences in clinical characteristics or variation in testing paradigms and tasks may account for the inconsistencies. This study aimed to assess several cognitive functions, including verbal declarative memory, working memory, verbal fluency and recognition memory for visuospatial information.

Methods: Thirty adults who met DSM-IV criteria for social phobia and 27 age- and gender-matched healthy controls aged between 18 and 65 years completed neuropsychological testing. Participants were recruited by means of newspaper advertisements. Severity of social phobia was rated using the Liebowitz Social Anxiety Scale. Participants completed a battery of neuropsychological tests including the Rey Auditory

Verbal Learning Test, spatial span, spatial recognition memory, spatial working memory, digit span, and verbal fluency and a verbal memory task comprising nonsense words. The National Adult Reading Test was used to estimate premorbid verbal IQ.

Results: There were no significant group differences on any domain of function, including verbal learning and memory, attention, working memory, verbal fluency, visuospatial functioning or psychomotor speed.

Conclusions: Social phobia was not associated with neuropsychological impairment, but clinical characteristics of the sample may account for this. Patients were high-functioning individuals with mild to moderate social phobia who had not specifically sought help for social phobia.

The multiscale hypothesis of bipolar disorder

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The brain is characterized by the presence of architectural structures – neurons, minicolumns, cortical columns – across a hierarchy of spatial scales. In addition, the activity of the brain is expressed – through action potentials, EEG oscillations, diurnal rhythms – across a multitude of temporal scales. We propose that bipolar disorder arises as a biological disturbance at a very fine spatial and temporal scale, within transmembrane dynamics, which then cascades across scales to be expressed at the slower scales of symptoms, episodes and ultimately the illness across the life span. This proposal is embedded within a hierarchical model of neocortical activity. Innovative data analysis methods, allowing the investigation of EEG and functional magnetic resonance imaging data from such a multiscale perspective, are presented. We hence propose a set of functional neuroscience experiments that would allow this ‘multiscale hypothesis’ of bipolar disorder to be tested.

Referential delusions of communication and self-monitoring deficits in psychosis

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Background: Although delusions of reference are one of the most frequently occurring symptoms of