COMT MODULATES WORKING MEMORY AND IMPULSIVITY CONTROL IN BIPOLAR DISORDER

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Introduction

Cognitive impairment is widely reported as a trait-like feature of the Bipolar disorder (BD), with main deficit in the domains of attention, working memory and executive function [1, 2] which involve the prefrontal cortex. However, the genetic basis of such impairments are still not fully elucidated. Recent data show that the polymorphism rs4680 of the COMT gene (encoding for the catechol-O-methyltransferase enzyme), also known as Val158Met, is responsible for genetically modulating dopaminergic levels in the prefrontal cortex and for this reason is a likely candidate to play a role in the neurobiology of cognitive disorders [3]. Current data seem suggest that this polymorphism exerts effects on cognition in subjects with schizophrenia and in healthy controls but there are fewer studies on BD and findings are inconclusive [4].

Aim of the study. The present study investigated the role of COMT polymorphism rs4680 on cognition and control functions in BD with tasks assessing working memory and emotional inhibition.

Methods

Subjects. 42 Bipolar patients (27 females, mean age = 44.26 years) and 99 healthy controls (66 females; mean age= 32.31 years) were enrolled in the study. Neurocognition. The “Brief Assessment of Cognition in Affective Disorders” (BAC-A) was carried out to all subjects, in particular working memory was assessed with a digit sequencing task and impulsivity with an emotional inhibition task with neutral and affective words. Genotyping. All subjects were typed for the single nucleotide polymorphism rs4680; the COMT variant as AA (Met/Met), GG (Val/Val) or AG (Val/Met) were evaluated by allelic discrimination systems by using quantitative PCR (Applied Biosystems). Statistical analysis. The statistical analysis were performed using the SPSS software. The raw scores obtained by the subjects at each subtest were entered as dependent variables in Multivariate analysis of variance (MANOVA) with ‘Group’ (BD and HC) and ‘COMT’ variant (GG, AA, AG) as between subjects’ fixed factors.

Results and Discussion

MANOVA. Main effect of ‘Group’ - BD reported significantly lower scores than HC in all the tasks (all p<0.0001) but the Affective Interference (p<0.05). Significant interaction Group x COMT variant in Number sequencing (p<0.048) and in Emotional Inhibition, with neutral (p<0.038) and affective words (p=0.042). No significant main effect of COMT variant (p>0.05).

POST-HOC COMPARISONS (All 2-tailed t-tests, α = 0.006 Bonferroni corrected). NOTE: HC subgroups did not differ between each other at Number Sequencing and Emotion Inhibition Neutral and Affective (all p>0.05). So their data were merged together for comparisons with BD subgroups.

Number Sequencing. Comparisons between BD subgroups. BD – AA did better than both BD – GG (p=0.012) and BD – AG (p=0.037), although not passing the more severe Bonferroni correction. BD – AG and BD – GG did not differ (p>0.05). Comparisons between BD subgroups and HC. Both BD – GG and BD – AG did worse than HC (both p<0.000). BD – AA performed at same level as HC (p>0.05).

Emotion Inhibition – Neutral and Affective. Comparisons between BD subgroups. BD – AA did better than BD – GG with both Neutral and Affective words (p=0.025 and p=0.023, respectively) although not passing the more strict Bonferroni correction. BD – AG did not differ form BD – AA and BD – GG (all p>0.05). Comparisons between BD subgroups and HC. BD – AA, BD – GG and BD – AG all reported poorer performances than HC with both Neutral and Affective stimuli (all p ≤ 0.003).

Conclusions

The present study shows that BD patients are generally impaired in several cognitive domains, although only BD carriers of allele G from COMT SNPs rs4680 show deficits in working memory and impulsivity control. This is compatible with previous evidences [3] and suggest that allele G can be a potential the targets for future innovative pharmacological medications. It would also be interesting to explore how personality traits or stress affect this genetic modulation in BD.

No potential conflict of interest

References

COMT modulates working memory and impulsivity control in bipolar disorder


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Introduction: Cognitive deficits are commonly reported in bipolar disorders (BD), mainly involving the domains of attention, working memory and executive functions [1]. However, the genetic basis of such impairments is still not fully elucidated. In this line, catechol-o-methyltransferase (COMT) has been suggested to be involved [2,3]. It contains the functional polymorphism Val108/158Met (rs4680) that results in two common variants of the enzyme (Val and Met). This polymorphism is responsible for modulating dopaminergic levels in the pre frontal cortex (Val being associated with higher activity).

Aim of the study: In the present study we investigated the role of COMT on cognition and control functions in BD with tasks assessing working memory and emotional inhibition.

Methods: The Brief Assessment of Cognition in Affective disorders (BAC-A) was administered to 42 BD patients (27 females, mean age = 44.26 years) and 99 healthy controls (HC) (66 females; mean age = 32.31 years). The single nucleotide polymorphisms COMT SNPs rs4680 were expressed and all the subjects were typified for the COMT variant as AA (Met/Met), GG (Val/Val) or AG (Val/Met). The statistical analyses were performed using the SPSS software. The raw scores obtained by the subjects at each subtest of the BAC-A were entered as dependent variables in Multivariate analysis of variance (MANOVA) with ‘Group’ (BD and HC) and ‘COMT_variant’ (GG, AA, AG) as between subjects' fixed factors. The MANOVA does not need p value adjustment.

Results: The analyses showed a significant main effect of ‘Group’ for almost all the tasks administered, with patients reporting the lower scores (all p<0.0001). In the Number Sequencing task, beside the main effect of ‘Group’ (p<0.0001), a significant main effect of the COMT variant emerged (p=0.038), together with a significant interaction Group x COMT_variant (p=0.048). As a whole, the BD group obtained lower scores than HC. However, post-hoc Bonferroni corrected t-tests revealed that BD in the AA COMT_variant subgroup performed at the same level as all the HC subgroups (p>0.05) while the BD in GG and AG subgroups did worse than both all HC and BD in AA group (all p<0.005). There were no differences between COMT_variant subgroups within HC. Also, a main effect of ‘Group’ (all p<0.0001) and a significant interaction between ‘Group’ and ‘COMT_variant’ emerged in Emotional Inhibition with both neutral (p=0.038) and affective words (p=0.042). All the three BD subgroups (i.e. AA, GG and AG) performed worse than controls. Moreover the post-hoc t-tests (Bonferroni corrected) showed that BD patients in GG subgroup had significantly poorer performance than BD in the AA subgroup at the Emotional Inhibition task with both neutral (p=0.038) and affective words (p=0.042). As a whole, the BD group obtained lower scores than HC. However, no differences between HC COMT_variant subgroups.

Conclusions: Compatibly with few previous investigations, the present study shows that only BD carriers of allele G from COMT SNPs rs4680 present deficits in working memory and impulsivity control, being potentially the targets for future innovative pharmacological medications. It would also be interesting to explore how personality traits or stress impact on such genetic modulation in BD.


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Keywords
Bipolar disorders
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