

COMT Moderation of the Association between Momentary Stress and Psychotic-Like Experiences in Daily Life

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Background

Daily life stressors play an important role in the expression of **psychotic-like experiences (PLEs)** and **paranoid symptoms** (1). Individual variation in PLEs in response to stressors is likely to be moderated by genetic variability. In particular, evidence suggests that the single nucleotide polymorphism (SNP) **Val158Met on the Catechol-O-Methyltransferase (COMT)** gene may moderate the association between **momentary stress** and psychosis given its role in dopaminergic regulation, which is relevant for both stress and psychotic reactivity (2).

There are **inconsistent results** regarding the direct association of Val158Met with risk of psychosis, possibly due to the need of considering how it moderates individuals' responses to environmental factors. However, there is scant information regarding the role of COMT in the real-world expression of PLEs and paranoid symptoms (3).

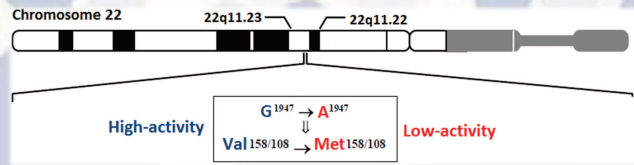


Figure 1. COMT Val158Met, involves a valine-to-methionine substitution at codon 158, that results in two common allelic variants (4).

Aims and Hypothesis

The present study employed **Experience Sampling Methodology (ESM)** to assess **gene-momentary environment interactions** in daily life in a non-clinical sample of Spanish young adults. It was examined:

- (1) whether appraisals of **stress** in general, and **social stress** in particular, were associated with **momentary PLEs and paranoia in daily life**, and
- (2) whether **COMT variability** moderated the association of general and **social stress with momentary PLEs and paranoia**.

Methods

Participants

A total of **201 undergraduate** students were recruited from the Universitat Autònoma de Barcelona (Spain). The mean age of the sample was 21.3 years (*SD* = 2.4).

The COMT Val158Met genotype distribution in the whole sample was 18% Met/Met, 47% Val/ Met and 35% Val/Val in **Hardy-Weinberg equilibrium**.

Experience Sampling Methodology (ESM)

ESM is a structured diary technique in which participants are prompted randomly eight times daily for one week to complete brief assessments of their current symptoms and experiences on 7-point Likert scales. Subjects were provided personal digital assistants.

Social Stress

I am alone because people do not want to be with me



Paranoia

Right now I feel suspicious

Right now I feel mistreated

Figure 2. ESM model

Results

(1) **Stressful situations and social stress were associated with momentary PLEs** ($\gamma_{10}=0.036$, $SE=0.004$, $p<.001$; $\gamma_{10}=0.084$, $SE=0.019$, $p<.001$, respectively) and **paranoia** ($\gamma_{10}=0.080$, $SE=0.010$, $p<.001$; $\gamma_{10}=0.157$, $SE=0.049$, $p<.001$, respectively).

(2) Cross-level interactions indicated that **COMT Val158Met genotype** did not moderate the association of stressful situations with PLEs or paranoia, whereas for **social stress**:

- The association between **perceived social rejection** and PLEs was higher for individuals with **the Val/Val genotype** as compared with those with the **Met/Met genotype** ($\gamma_{12}=-0.109$, $SE=0.051$, $p<.05$).

- Similarly, the association between **perceived social rejection** and **paranoia** was higher for individuals with the **Val/Val genotype** than for **Met carriers** ($\gamma_{11}=-0.265$, $SE=0.134$ $p<.05$; $\gamma_{12}=-0.290$, $SE=0.143$, $p<.05$).

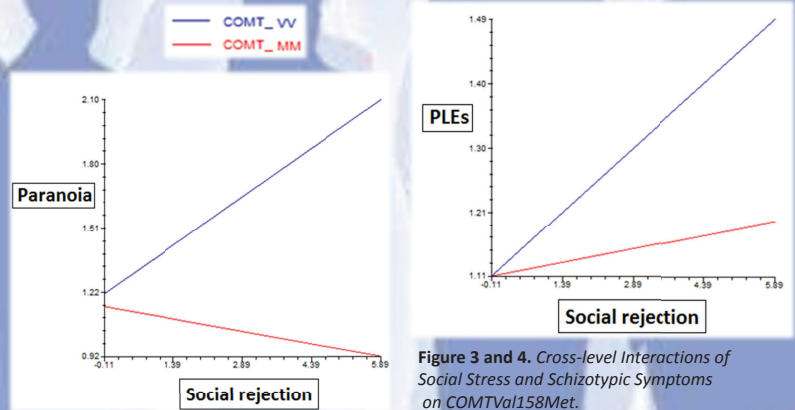


Figure 3 and 4. Cross-level Interactions of Social Stress and Schizotypic Symptoms on COMT Val158Met.

Additionally, when participants were with others at the time of the signal, **perceived social distance** ($\gamma_{10}=-0.009$, $SE=0.003$, $p<.001$) and **preference to be alone** ($\gamma_{10}=0.021$, $SE=0.004$, $p<.001$), other social-stress appraisals, were more strongly associated with PLEs for Val/Met than for Val/Val participants ($\gamma_{11}=-0.011$, $SE=0.005$ $p<.05$; $\gamma_{11}=-0.021$, $SE=0.008$, $p<.01$, respectively).

Discussion

Consistent with the **stress-sensitivity model** (5), momentary stress was associated with momentary PLEs and paranoid experiences.

The **COMT Val158Met genotype only moderated the psychotic and paranoid response to environmental social stress**, but not the associations with situational stress. Although a mixed pattern emerged in terms of the **genotypic profile** conferring a higher psychotic-like response to social stress appraisals, the **findings are consistent with the increasing relevance given to socially defeating schemas** in the experience of reality distortion. Our findings seem to be partially in agreement with a few studies conducted in population samples where the **Val allele has been associated with social stress-induced psychotic experiences and paranoia** (6). It has been hypothesised that the prefrontal hypodopaminergia associated with the Val/Val genotype (7, 8) may facilitate the disinhibition of mesolimbic dopamine in the face of stress and thus increase psychotic reactivity.

Further studies, especially in at-risk populations, are needed to resolve the apparently contrasting findings. In addition, **interactions with other SNPs that may influence dopaminergic activity, such as DAT and MTHFR** (9), should be taken into account to provide a complete overview of the effects of COMT on subjective stress, suggesting the need to examining GxG interactions.

References

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