Dopamine transporter gene (DAT1) and depressive symptomatology are associated with response in a self-referential encoding task

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Background

The Dopamine Transporter Genetic Polymorphism (DAT1)

– The DAT gene codes for a dopamine transporter, which transports dopamine into presynaptic terminals in the brain[1].

– VNTR (Variable Number Tandem Repeat) variants exist for DAT1, with 9-repeat and 10-repeat (9R and 10R) most common; the 9R/9R genotype appears to be associated with reduced vulnerability to depression[2]. DAT1 is associated with dopamine availability, which appears to mediate cognitive functioning[3].

– DAT1 has been linked with variability in negative emotionality, alongside other more commonly-studied genes that are associated with depression and other mental illness[1,2]. The dysfunction of the brain's dopamine transportation is strongly connected to depressive symptoms. It is implicated in impaired cognitive functioning, perhaps resulting from differential regulation of dopamine[1].

– The interaction of DAT1 and depressive symptoms can be used as a predictor for behavioral responses to measures of negative schemata.

The Self-Referent Encoding Task (SRET)

– The SRET[4,5] is an affective decision-making task that asks participants to determine whether computer presented words are self-referential.

– These words are positively- and negatively-valenced. Thus, reaction times (RT) can be measured to determine how well these words fit participants' schemata relating to their selves. Cognitive vulnerability is indicated by quicker RTs in response to negative self-referent adjectives, or to positive non-self-referent adjectives.

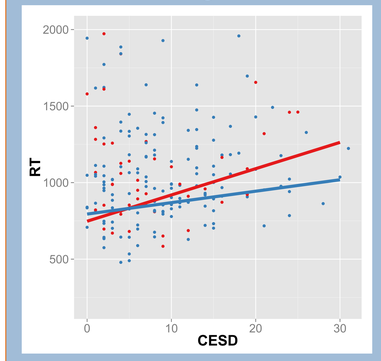
– Negative self-referent processing has been associated with depression[6].

Our Hypothesis

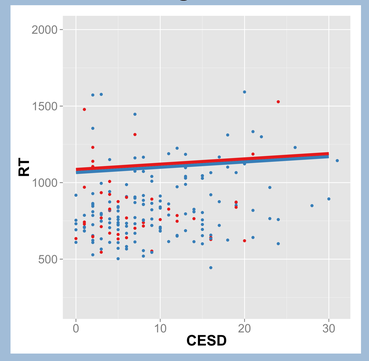
– Individuals with the 9R polymorphism will show slower RTs to negative adjectives deemed self-referential and to positive adjectives deemed not to be.

Results & Discussion

A. How DAT1 moderates RT to self-referent, negative words

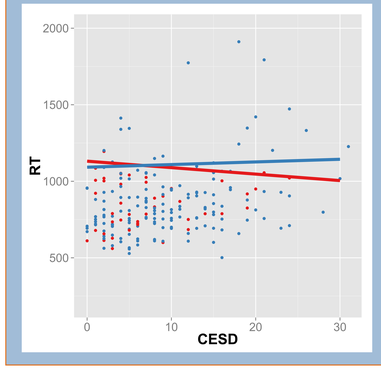


B. How DAT1 moderates RT to non-self-referent, negative words

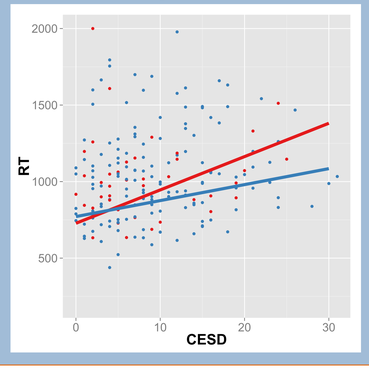


Group: 9R; non-9R

C. How DAT1 moderates RT to self-referent, positive words



D. How DAT1 moderates RT to non-self-referent, positive words



– There is a significant 4-way interaction between DAT1 (gene), CESD (depressive symptoms), SRET valence, and SRET reference in predicting RT on the task, b = -27, t (591) = -1.99, p < .05. The model is significant, χ^2 (1) = 4.040, p < .05.

– This interaction suggests that carriers of the 9R VNTR of DAT1 perform significantly differently from non-carriers in the manner in which CESD score interacts with SRET conditions. A contrast of grouped [self-referent / negative and non-self-referent / positive] conditions by [non-self-referent / negative and self-referent / positive] conditions, found significant effects for 9R/non-carrier comparisons across group: z (280.96) = 3.74, p < .01 and z (280.96) = 3.914, p < .01.

– The model is driven by subjects at high levels of depressive symptoms. At low levels (CESD < 16) only, the model does not hold, χ^2 (1) = 0.767, p > .1.

– When CESD is covaried out, DAT1 alone does not interact with SRET condition to predict performance on the SRET. DAT1 is not associated with CESD score, although it has been shown to interact with negative affect in the past[7].

– Recent work has found that COMT polymorphisms associated with reduced vulnerability are associated with likelihood in recalling positive self-referent words following the SRET[8]. In this sample, DAT1 is not associated with word recall in any condition. Further work may explore links between DAT1 and other behavioral tasks, as well as gene interactions.

– The results described herein suggest that the DAT1 9R VNTR may aid resilience against cognitive bias, at higher levels of depression.

Method

– Adult participants were recruited from the Austin community.

– N = 201 (113 female, mean age 25.1 (4.3))

– Participants were screened for presence of Axis I disorders, but nonetheless displayed a range of levels of depression symptomatology (CESD range from 0-31).

– Assessments included the SRET, the Center for Epidemiological Studies Depression inventory (CESD, a self-report measure of depression), and a saliva sample collected for genetic assay. Genetics were analyzed at the lab of the second author.

– SRET was conceptualized as having four conditions: self-referent words that were either positive or negative, and the same for non-self-referent words.

– Mixed model linear regression was used to test the interaction between the independent variables in predicting RTs on the SRET. Carriers of the 9R VNTR variants (N = 45) were grouped separately from non-carriers (N = 156). Regression lines were plotted over scatterplots of the data, grouped by condition on the task.

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