

INTRODUCTION:

Catechol-O-methyltransferase (COMT) is a gene that influences the amount of dopamine active in synapses of the human prefrontal cortex (PFC), the region of the brain most crucial for working memory. There are two alleles for this gene, Met and Val. Met codes for a less effective enzyme than Val, leading to higher levels of dopamine in the PFC. These higher levels of dopamine may be associated with heightened cognitive performance and neural efficiency (Malhotra et al., 2002).

On the other hand, Externalizing behavior (e.g. impulsivity, aggressiveness, and substance abuse) has been associated with poorer cognitive performance. Our study investigates whether or not the Met/Val polymorphism moderates the relationship between externalizing behaviors and neural activity during a working memory task. A similar effect has been demonstrated with an easier cognitive task (Shehzad et al., 2012).

HYPOTHESIS:

Our hypothesis is that we will find an interaction between the Val/Met polymorphism and endorsement of Externalizing behavior **in** predicting neural activity. Specifically, participants with high Externalizing behavior should show slower neural activation than those with low externalizing behaviors, especially if these participants had the Val/Val genotype.

METHODS:

An urban community sample was collected (N=270) and subjects underwent an fMRI scan. During the scan the subjects completed a working memory task (N-Back.) Subjects also completed the Externalizing Spectrum Inventory (ESI) and provided saliva samples that have been genotyped. We analyzed the working memory task using the FMRIB Software Library (v5.0). We are including Val/Met in the analysis to test whether or not it moderates the relationship between Externalizing behavior and neural activity during performance of the N-Back task.

CONSTRUCTS:

EXTERNALIZING BEHAVIOR:

'Externalizing' refers to the tendency to externalize (i.e. outwardly express), and Externalizing Behavior is characterized by outwardly expressing maladaptive emotions and thoughts. It is connected to issues with impulse control, destructive aggression, rebelliousness, and irresponsibility. The tool that we used to measure Externalizing behavior is the ESI, which includes 160 items rated by participants on a 4-point scale.

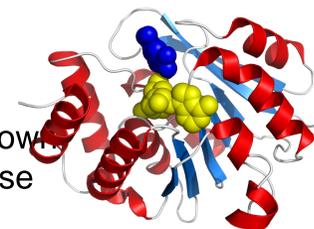
N-BACK TASK:

Subjects completed both 2-back and 0-back tasks during an fMRI scan. In the 2-back condition, subjects were instructed to press a button if a word on the screen in front of them appeared two words back or if the shape on the screen appeared two shapes back. For the 0-back condition, subjects pressed the button if the letters were capitalized (vs lowercase) or if they were blue (vs green). We collected images of the brain while subjects were performing the task, and our main focus will be comparing the 2-back condition to rest.

This task is the "working memory" portion of the study, and it is also a measure for cognitive performance, as it correlates strongly with IQ.

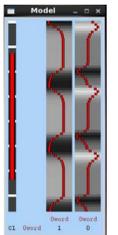
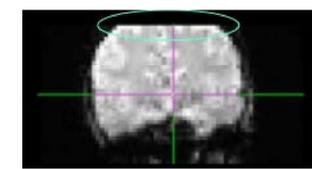
COMT/GENETICS:

COMT (pictured right) is an enzyme responsible for breaking down dopamine in the PFC. It can be expressed as either Met/Met, Met/Val, or Val/Val. Research has shown interesting implications based on these allele combinations.



PROGRESS:

(1) **QUALITY CONTROL:** Before beginning any analysis, we had to go through our original pool of 270 subjects and look through each of their fMRI scans. Each subject had four scans, so the total number of images was 1080. We excluded subjects who moved too much in the scanner, as well as subjects whose brains were not scanned properly (i.e. parts missing from the image). An example of an excluded subject can be seen below (left). We excluded thirteen subjects.



(2) **LOWER LEVEL:** We used a block design to conduct our lower level analysis, in which activation across each set of trials is compared to intervening periods of rest. Above (right) you can see a visual representation of the block design in FSL.

(3) **HIGHER LEVEL:** The higher level analysis will combine subjects and allow us to compare each condition for each subject to all the other subjects. This is also where we add our measures and covariates to see if activation patterns are related to any of our other measures.

ANTICIPATED RESULTS & DISCUSSION:

We predict that the Met/Val allele will moderate the negative relationship between externalizing behaviors and cognitive performance. That is, the COMT gene will affect the strength of the relationship between ESI scores and neural patterns. Understanding these neural and genetic factors that contribute to risk for these behaviors is a crucial goal for clinically oriented psychological research.

REFERENCES:

- Malhotra, A. K., Kestler, L. J., Mazzanti, C., Bates, J. A., Goldberg, T., & Goldman, D. (2002). A functional polymorphism in the COMT gene and performance on a test of prefrontal cognition. *American Journal of Psychiatry*, 159(4), 652-654.
- Shehzad, Z., DeYoung, C. G., Kang, Y., Grigorenko, E. L., & Gray, J. R. (2012). Interaction of COMT val 158 met and externalizing behavior: Relation to prefrontal brain activity and behavioral performance. *NeuroImage*, 60(4), 2158-2168.

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