Effects of Genes on Individual Differences in Executive Function Development in Preschool-Aged Children

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Introduction

Many studies have examined the relationship between normative individual genetic polymorphisms and executive function skills (attention shifting, working memory, inhibitory control) in adults.

Since executive function skills depend on the brain's prefrontal cortex, variability in genes that impact neurotransmitter function in this region should relate to individual differences in cognitive capabilities.

Two genetic variants, both of which influence the level of the neurotransmitter dopamine in the prefrontal cortex, that have been linked to individual differences in executive function in adults include:

- *Catechol-o-methyl transferase* ***(COMT) Val158Met polymorphism***: the Met allele is associated with better performance on tasks requiring sustained attention; the Val allele is advantageous for tasks requiring updating
- *Dopamine active transporter gene 1 (DAT-1) variable number tandem repeat* ***(DAT-1 VNTR)***: 10-repeat carriers show higher levels of risk-taking and impulsivity

Given widespread changes in the brain's dopamine system over development, the effects of these genotypes may vary by age. However, few studies have examined how individual differences in genes related to the brain's dopamine system impact the development of higher-level cognitive skills in young children.

Question

Do individual differences in the COMT Val158Met and DAT-1 VNTR polymorphisms predict the development of executive functions at age 5?

Participants

Inclusion Criteria: Forty-three 5-year-old children were recruited from a sample previously tested during infancy by Markant et al. (2010). At 5-years of age children were additionally screened for known developmental or neurological disorders, and known vision or hearing impairments.

Genotyping: Genotyping for the COMT Val158Met and DAT-1 VNTR polymorphisms was completed as described in Markant et al. (2010) using buccal swabs collected when participants were infants.

N = 43	COMT Any Val allele	COMT Met/Met allele	DAT-1 VNTR 9/10 repeat	DAT-1 VNTR 10/10 repeat
Sex	16 f, 13 m *n* = 29	4 f, 7 m *n* = 11	9 f, 8 m *n* = 17	9 f, 11 m *n* = 20

Demographics: Children were predominantly Caucasian (85%), with most households having at least one parent who had completed a college-degree or higher.

Acknowledgments

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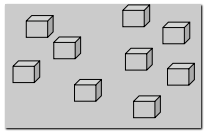
Methods

***Working Memory Tasks*:**

I-Spy Memory Search Task:
Children are presented with a target animal, and were then shown a scene with four animals. Children were asked whether the target animal was present in the picture. Memory load was increased by requiring children to remember multiple targets. Accuracy at detecting targets and rejecting non-targets was measured.

Corsi Block Task:
Children are asked to repeat a sequence of tapped blocks with their index finger. Cubes are touched at a rate of 1 cube/second. Forward and backward spans were measured.



***Inhibitory Control Tasks*:**

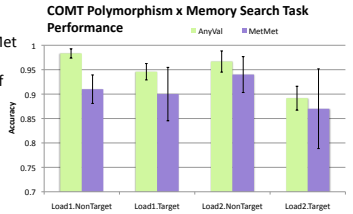
Delayed Choice Task:
Children were given repeated opportunities to choose a small reward (stickers or M&Ms) now, or wait to receive a larger reward later. Percentage of delayed choices was measured.

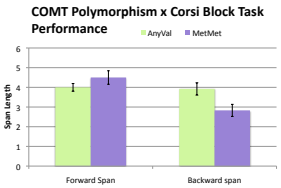
Balloon Analogue Risk Task (BART):
Children were given the chance to earn coins by blowing up a balloon by pressing the balloon on the screen. Coins were presented after each press, and could be saved before the balloon popped. The average number of pumps on unexploded balloons was measured, with higher scores reflecting greater risk-taking and poorer inhibition.

***Parent Questionnaires*:** Parents completed the Behavior Rating Inventory of Executive Function- Preschool Version (BRIEF-P), the Strengths and Difficulties Questionnaire (SDQ), and the Child-Behavior Questionnaire (CBQ).

Results: COMT & Working Memory

• *Memory Search task*: The COMT Met/Met group performed worse at rejecting non-targets ($p < .01$), and showed a pattern of poorer performance across all other trial types.

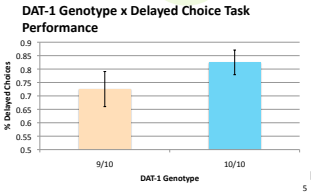




• *Corsi Block task*: The COMT Met/Met group performed worse on backwards span ($p < .04$).

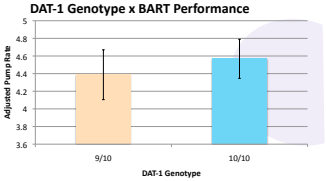
***Overall*, the COMT polymorphism predicted individual differences in working memory abilities at preschool age, with Met/Met carriers performing more poorly.**

Results: DAT-1 & Inhibitory Control



• *Delayed Choice task*: There was a non-significant relationship between children's performance and DAT-1 VNTR genotypes.

• *BART task*: There was a non-significant relationship between children's performance and DAT-1 VNTR genotypes.



***Overall*, the DAT-1 VNTR polymorphism did not predict individual differences in inhibitory control development at preschool age.**

Results: Parent Report by Genotype

• *Parent report* of children's inhibitory control, working memory development, and overall executive function skills was unrelated to children's genotypes.

Discussion

We found evidence that the Val allele of the COMT Val158Met polymorphism predicts better working memory performance at preschool age, while variation in the DAT-1 gene was unrelated to inhibitory control.

- *On both working memory tasks, children homozygous for the Met allele performed more poorly than their peers with a Val allele, suggesting that effects of the COMT polymorphism on working memory are present early in development.*
- *Neither DAT-1 VNTR polymorphism predicted individual differences in children's inhibitory control, suggesting that environmental factors may have a stronger impact on inhibitory control development during early childhood. Additionally, the small sample size for this candidate gene study may have impacted our ability to detect effects of this polymorphism early in development.*
- *Parent report of inhibitory control and working memory development was not related to children's genotype, indicating that any differences observed by genotype are not within the clinical range of abnormality.*

This study contributes to our understanding of the biology of individual differences in children's executive function development.

Future studies should investigate intervention efforts appropriate for children who are at higher risk for atypical executive function development. These efforts may be particularly valuable during early childhood when the brain's dopamine system is at highest plasticity.

Conclusion

Similar to previous studies conducted with adults, individual differences in children's working memory skills at age 5 were related to polymorphisms in genes affecting the brain's dopamine system.