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

<table>
<thead>
<tr>
<th>Sex</th>
<th>Any Val allele</th>
<th>COMT Met/Met allele</th>
<th>DAT-1 VNTR 9/10 repeat</th>
<th>DAT-1 VNTR 10/10 repeat</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 f, 13 m</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 f, 7 m</td>
<td>n = 11</td>
<td>9 f, 8 m</td>
<td>n = 17</td>
<td>9 f, 11 m</td>
</tr>
</tbody>
</table>

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

Acknowledgments

This research was supported by a University of Minnesota Graduate School Fellowship and Doctoral Dissertation Fellowship, and by the National Institute on Aging P30 AG010129 (PhD training at the University of Minnesota) and the National Institute of Mental Health R01 MH082480 (principal investigator, Kathleen M. Thomas). Support for the I-SPY Memory Search Task was provided by the Elyse T. Stahl Endowment in Behavioral Development. The authors thank the families of the participants and members of Kathleen M. Thomas’ Cognitive Development & Neuroimaging lab.

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 homoygous 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.