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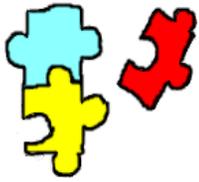
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Genes and Behavior in Preschool Children: The Relation between Dopamine Genotype and Latent Executive Control

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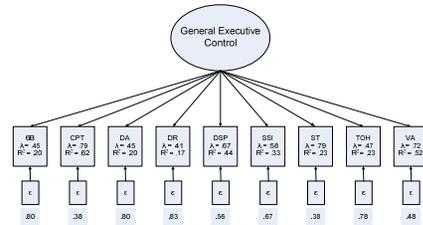


Dopamine and Executive Control

- Dopaminergic neurotransmission is implicated in the executive control of cognition and behavior (Braver & Cohen, 2000)
- The prefrontal cortex is thought to modulate activity in other brain regions through "bias signals" boosting activation of task-relevant neural pathways, likely through the action of dopamine (Montague, 2004)
- A number of studies have found associations between executive control and dopamine-related candidate genes, likely because of variation in the availability of dopamine in the synapse and/or efficiency of dopaminergic neurotransmission (Casey, 2002; Roesch-Ely, 2005)
- Furthermore, dopamine genotype has been found to relate to attention problems and attention deficit/hyperactivity disorder (ADHD; Faraone, 2005)
- A better understanding of how variation in dopamine genotype relates to children's regulation of attention and behavior has significance for clinical practice and possible intervention

Latent Executive Control

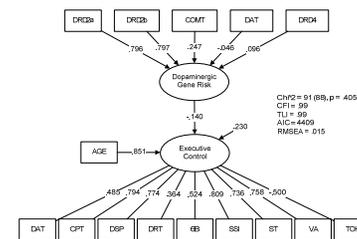
- A latent variable approach has been shown to be particularly useful for studying executive control, in that it results in a "purified" measure that capture common variance across executive control tasks that differ in their non-executive demands (Miyake, 2000)
- Performance on the executive control battery was used to construct a latent variable indexing executive control (Wiebe, Espy, & Charak, under review)



- Next, the relationship between dopamine genotype and latent and executive control was explored using structural equation modeling, in Mplus Version 4.1 (Muthén, 2006).

Genes and Executive Control: Model 2

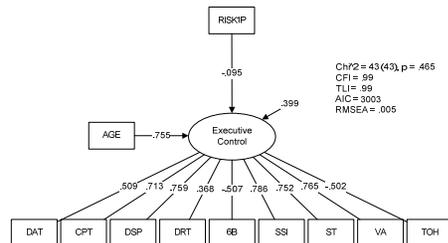
- To look at the contributions of individual genes, individual dummy variables were used to create a latent Genetic Risk variable, in a Multiple Indicator Multiple Cause (MIMIC) model



- This model also demonstrated good fit to the data, as evidenced by a non-significant chi-square test
- However, the effect of genetic risk was statistically significant ($p < .05$)
- As shown by the loadings of the individual genetic risk dummy variables on the Genetic Risk latent variable
- The effect can be largely attributed to DRD2 and COMT, as model results do not change substantially when DRD4 and DAT are dropped

Genes and Executive Control: Model 1

- First, a summary variable was calculated by simply adding up "risk scores" for all dopamine genes of interest
- This risk score was used to predict latent executive control
- Age was also included as a covariate, to account for age differences in executive control



- While this model demonstrated good fit to the data, the effect of genetic risk did not reach significance ($p = .15$), although the effect was in the predicted direction (higher genetic risk was related to poorer executive control)

Discussion

- We observed a relationship between dopamine genotype risk score and latent executive control in preschool children:
 - Children with alleles of dopaminergic genes that have been previously shown to relate to poorer outcomes had lower values on an Executive Control latent variable.
 - This effect seems to be specific to DRD2 and COMT.
- This study also further demonstrates the utility of a latent variable approach in the study of preschool executive control.
- These results are consistent with differences in dopamine availability and efficiency of neurotransmission related to different dopamine alleles.
- Further work is necessary to test this relationship in a larger sample, and to examine the contributions of gene-environment and gene-gene interactions to executive control development
- Given that executive control problems are implicated in ADHD (Nigg, 2005), these findings may shed light on how genetic risk contributes to behavioral problems.

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Dopamine Gene Alleles associated with Risk

| Gene | Risk Allele |
|-------------------------------------|---|
| COMT (catechol-O-methyltransferase) | Val allele: associated with higher activity/lower dopamine availability, poorer Wisconsin Card Sorting Test performance (Egan, 2001), increased cortical activation in a working memory task (Bertolino, 2006) |
| DAT (dopamine transporter) | 10-repeat allele: associated with lower caudate volume (Durston, 2005), increased impulsivity in children with ADHD (Kim, 2006), increased cortical activation in a working memory task (Bertolino, 2006) |
| DRD2 (D2 dopaminergic receptor) | A1 allele: associated with lower receptor availability in striatum, lower inhibitory control (Rodriguez-Jimenez, 2006), increased susceptibility to addiction (Munafò, 2004), and neural response to reward (Cohen, 2005) |
| DRD4 (D4 dopaminergic receptor) | 7 repeat allele: associated with poorer sustained attention (Kieling, 2006), novelty-seeking in males (Laucht, 2006), increased vulnerability to the effects of harsh parenting (Bakermans-Kranenburg, 2006) |

Method

- 133 preschool children (mean age 4 years 1 month, range 2.5 to 6 years) were administered an executive control battery that included the following tasks: Delayed Alternation, Continuous Performance Task, DAS Digit Span, Delayed Response, Six Boxes, Shape School, NEPSY Statute, NEPSY Visual Attention, and Tower of Hanoi
- Children were genotyped on the COMT, DAT, DRD2, and DRD4 polymorphisms of interest from cheek swabs obtained using a preschooler-friendly "lollipop game" procedure (Espy, 2002)
- Children were assigned dummy codes of 0 or 1 for each gene, where 1 indicated the presence of the "risk allele"