

*Developmental Cognitive Neuroscience Laboratory*  
*Developmental Cognitive Neuroscience*  
*Laboratory - Faculty and Staff Publications*

---

University of Nebraska - Lincoln

Year 2006

---

Genetic bases of executive control in  
preschool children: TRAILS-P  
performance is related to DRD2 genotype

S. A. Wiebe      M. Y. Chang      J. Huggenvik

T. Jameson      K. A. Espy

# Genetic Bases of Executive Control in Preschool Children: Trails-P Performance is Related to DRD2 Genotype



Sandra A. Wiebe, Ph.D.<sup>1</sup>, Moh Yin Chang, M.S.<sup>1</sup>, Jodi Huggenvik, Ph.D.<sup>2</sup>, Travis Jameson, B.S.<sup>2</sup>, & Kimberly Andrews Espy, Ph.D.<sup>1</sup>  
 1. Developmental Cognitive Neuroscience Laboratory, Psychology/Office of Research, University of Nebraska-Lincoln  
 2. Department of Family and Community Medicine, Southern Illinois University Carbondale

## Dopamine and Executive Control

- Miller and Cohen's (2001) model of executive control emphasizes the prefrontal cortex's modulation of 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 (Blasi, 2005; de Frias, 2005)
- Variation in the D2 dopamine receptor DRD2 has been linked to addiction (Munafò, 2004) and sensitivity to reward (Cohen, 2005); individuals with 1 or 2 copies of the A1 allele are at risk for negative outcomes
- However, several recent studies have linked DRD2 with executive control and the ability to adapt behavior to changing contextual contingencies in human adults (Rodríguez-Jiménez, 2006; Roesch-Ely, 2005) and in animal models (Kruzich, 2004)

## The Preschool Trail-Making Test

- In the Trail-Making Test, subjects connect stimuli on a page in sequence
- Condition A (Control): Subjects connect letters only
- Condition B (Switch): Subjects alternate between letters and numbers
- This task is sensitive to frontal dysfunction (Reitan, 1955)
- Because preschool children are still learning literacy skills, the adult version of the test is not a valid test
- In the Preschool Trail-Making Test (Trails-P), stimuli are a family of 5 dogs that vary in size (Espy, 2004)
- Children complete the task by using a happy face stamper to mark stimuli in order from smallest to biggest
- Condition A (Control): Children stamp dogs only
- Condition B (Switch): Children "feed" dogs by stamping dogs and bones alternately
- Condition C (Inhibit): Children stamp dogs only (ignore bones on page)



➤ Latency to complete each page and number of errors are scored

## Method

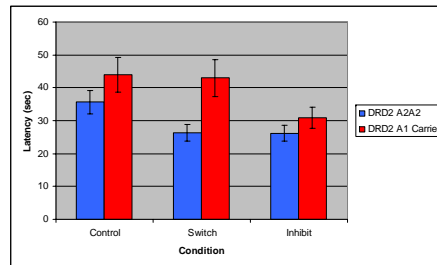
- 91 preschool children (mean age 4.3 years, range 2.5 to 6 years) were administered the Trails-P task as part of an executive control battery
- Children were genotyped on the DRD2 Taq1A polymorphism from cheek swabs obtained using a preschooler-friendly "lollipop game" procedure (Espy, 2002)
- Children were classified as DRD2 A1 carriers (A1A1 or A1A2) or non-carriers (A2A2)
- Demographic information for the full sample and the 2 genotype groups is presented in the table

	Total Sample (n=91)		A1A1 (n=2) or A1A2 (n=39)		A2A2 (n=50)	
	Mean	SD	Mean	SD	Mean	SD
Age	4.42 yrs	0.9 yrs	4.33 yrs	0.8 yrs	4.5 yrs	0.95 yrs
Sex (% male)	45 %	-	46 %	-	45 %	-
Household Income	\$39,534	\$58,772	\$29,768	\$22,156	\$47,634	\$76,400
Mother's Education	14.4 yrs	2.36 yrs	13.4 yrs	1.68 yrs	15.2 yrs	2.55 yrs
Father's Education	14.3 yrs	2.76 yrs	13.8 yrs	2.44 yrs	14.6 yrs	2.95 yrs

- All analyses included age as a covariate to control for developmental differences in Trails-P performance
- Children were included if they completed at least one condition of the Trails-P task

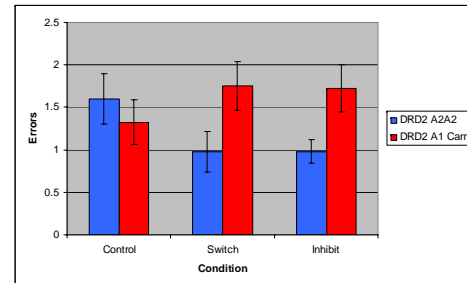
## Results: Response Latencies

- For latencies, there was a significant effect of genotype:  $F(1, 88) = 4.14, p < .05$
- There was also a main effect of condition:  $F(2, 88) = 6.76, p < .005$
- Tukey tests revealed that all the Inhibit condition differed significantly from the Control condition ( $p < .005$ ), and marginally from the Switch condition ( $p < .10$ ); the Control and Switch conditions did not differ
- The interaction between genotype and condition was not significant:  $F(2, 88) = 1.91, p > .15$



## Results: Errors

- For errors, there was a significant interaction between condition and genotype:  $F(2, 88) = 3.92, p < .05$
- The effect of genotype was insignificant for the Control condition ( $p = .44$ ), marginal for the Switch condition ( $p < .10$ ) and reached significance for the Inhibit condition ( $p < .02$ )
- Main effects of genotype and condition were not statistically significant ( $ps > .20$ )



## Discussion

- DRD2 genotype contributes to variation in executive control in young children, as indexed by the Trails-P task
- Deficits in executive control in DRD2 A1 carriers may be related to lower availability of dopamine receptors associated with this genotype
- For errors, gene-related differences were observed only for the Inhibit and, to a lesser degree, Switch conditions
- However, for response latencies, gene-related differences were seen across all 3 conditions, even though the Control condition was intended as a non-executive baseline
- It is possible that, for young children, even the control condition (sequencing dogs based on size) involved executive control
- Problematically, faster latencies were observed for more challenging conditions; this may be because children with strong executive control deficits may have been less likely to complete the later conditions because of difficulties understanding or complying with task instructions
- Furthermore, genotype groups differ somewhat in SES and parental education
- More work is necessary to test for replication in a larger sample, examining the contributions of gene-environment and gene-gene interactions to executive control development

## References

- Blasi, G., Mattay, V. S., Bertolino, A., Elvevag, B., Callicott, J. H., Das, S., Kolachana, B. S., Egan, M. F., Goldberg, T. E., & Weinberger, D. R. (2005). Effect of catechol-O-methyltransferase val158 genotype on attentional control. *The Journal of Neuroscience*, 25, 5038-5045.
- Cohen, M. X., Young, J., Baek, J.-M., Kessler, C., & Ranganath, C. (2005). Individual differences in extraversion and dopamine genetics predict neural reward responses. *Brain Research: Cognitive Brain Research*, 25, 851-861.
- de Frias, C. M., Annerbrink, K., Westberg, L., Eriksson, E., Adolffson, R., & Nilsson, L.-G. (2005). Catechol O-methyltransferase Val158Met polymorphism is associated with cognitive performance in nondemented adults. *Journal of Cognitive Neuroscience*, 17, 1018-1025.
- Espy, K. A., & Hamby, A. F. (2002). "Getting into the mouths" of preschoolers: A method for obtaining buccal samples for later genotyping. *Developmental Neuropsychology*, 21, 197-200.
- Espy, K. A., & Cwik, M. F. (2004). The development of a Trail Making Test in young children: The TRAILS-P. *The Clinical Neuropsychologist*, 18, 1-12.
- Kruzich, P. J., & Grandy, D. K. (2004). Dopamine D2 receptors mediate two-odor discrimination and reversal learning in C57BL/6 mice. *BMC Neuroscience*, 5:12.
- Miller, E., & Cohen, J. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, 24, 167-202.
- Montague, P. R., Hyman, S. E., & Cohen, J. D. (2004). Computational roles for dopamine in behavioural control. *Nature*, 431, 760-767.
- Munafò, M., Clark, T., Johnstone, E., Murphy, M., & Walton, R. (2004). The genetic basis for smoking behavior: A systematic review and meta-analysis. *Nicotine and Tobacco Research*, 6, 583-597.
- Reitan, R. M. (1955). The relation of the Trail Making Test to organic brain damage. *Journal of Consulting Psychology*, 19, 393-394.
- Rodríguez-Jiménez, R., Avila, C., Ponce, G., Ibanez, M. I., Rubio, G., Jiménez-Arriero, M. A., Ampuero, I., Ramos, J. A., Hoenicka, J., & Palomo, T. (2006). The Taq1A polymorphism linked to the DRD2 gene is related to lower attention and less inhibitory control in alcoholic patients. *European Psychiatry*, 21, 66-69.
- Roesch-Ely, D., Scheffel, H., Weiland, S., Schwanager, M., Hundemer, H.-P., Kohler, T., & Weisbrod, M. (2005). Differential dopaminergic modulation of executive control in healthy subjects. *Psychopharmacology*, 178, 420-430.

## Acknowledgments

This research was supported by NIH grants MH 065668, DA 014661, and HD 038051 to Kimberly Andrews Espy. We would like to thank Megan Banet, Mary Cwik, Abby Johnson, Heather Kaiser, and Jessica Martin for assistance with data collection, Matthew Moehr for assistance with data analysis and figure preparation, and the children and families who made this work possible. Correspondence regarding this poster may be addressed to Sandra Wiebe (swiebe2@unl.edu).