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

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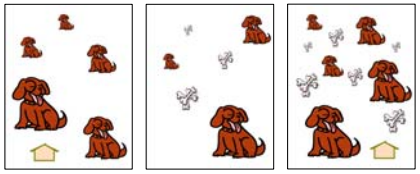
Dopamine and Executive Control

➢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 (Munafo, 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 (Rodriguez-Jiminez, 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

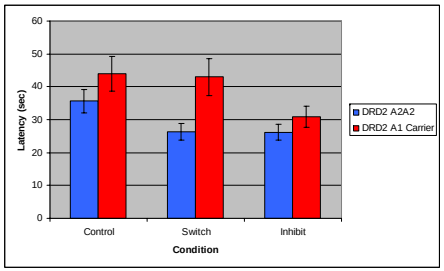
➢91 preschool children (mean age 4.3 years, range 2.5 to 6 years) were administered the Trails-P task as part of an executive control battery
➢Children were genotyped on the DRD2 Taq1A polymorphism from cheek swabs obtained using a preschooler-friendly "lollipop game" procedure (Espy, 2002)
➢Children 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

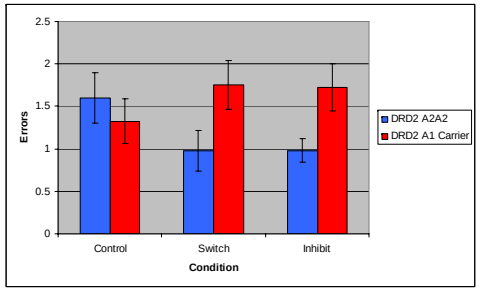
Results: Response Latencies

➢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

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Acknowledgments

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