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

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



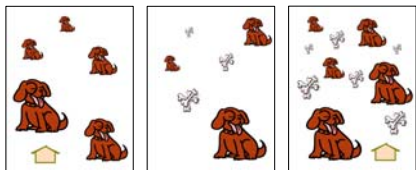
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## Dopamine and Executive Control

- 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 (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

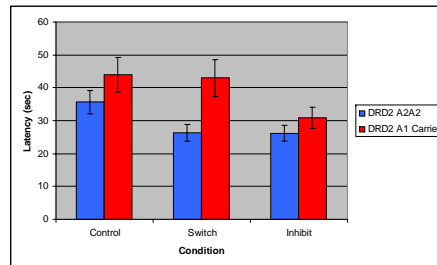
- 91 preschool children (mean age 4.3 years, range 2.5 to 6 years) were administered the Trails-P task as part of an executive control battery
- Children were genotyped on the DRD2 Taq1A polymorphism from cheek swabs obtained using a preschooler-friendly "lollipop game" procedure (Espy, 2002)
- Children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

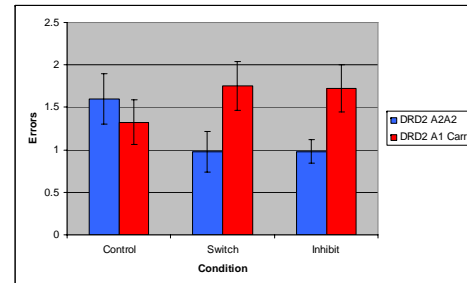
## Results: Response Latencies

- 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

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