Genetic Polymorphisms Contributing to Individual Differences in Infants' Selective Attention

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Introduction

Selective attention is an important contributing factor in infant learning as it can organize and limit the amount of potentially relevant stimuli from the environment. Spatial cueing paradigms can manipulate selective attention and present the phenomena called inhibition of return (IOR). Inhibition of return occurs when salient cues are followed by a relatively long delay and attention is biased towards items appearing in the opposite, non-cued location. Researchers have identified individual differences in this sensitivity to salient cues. These variations have been related to genetic differences among adults, especially in the cholinergic receptor (CHRNA4), catechol-O-methyltransferase (COMT), and dopamine transporter (DAT1) genes. Although previous studies have linked these genes to the development of Attention Deficit Hyperactivity Disorder (ADHD), many have failed to replicate their results due to the complexity of ADHD phenotypes. One alternative is to examine the effects of genotype on isolated component attention tasks rather than prematurely concluding that specific genotypes initiate the development of ADHD. The present study looks at the relationship between infants' attention responses during the IOR task and genetic polymorphisms in the CHRNA4, COMT, and DAT1 3'UTR genes.

Question

Do genetic polymorphisms relate to variation in infants' sensitivity to spatial cues?

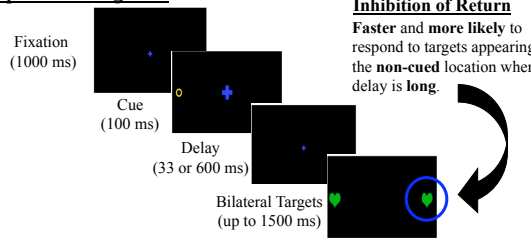
Methods

Participants: 64 7-month-old infants (32 M, 32 F) completed the spatial cueing task and provided a DNA sample.

DNA Sampling: Genetic samples were collected using a buccal swab and sent to an affiliated lab for genotyping of the following polymorphisms:

1. **Single-Nucleotide Polymorphisms (SNPs):** variation in nucleotides (A, T, C, G) at a single location –*CHRNA4 (rs1044396), COMT (Val158Met)*
2. **Variable-Number Tandem Repeat (VNTR):** a segment of nucleotide sequence repeats a variable number of times – *DAT1 3'UTR*

Spatial Cueing Task



Inhibition of Return

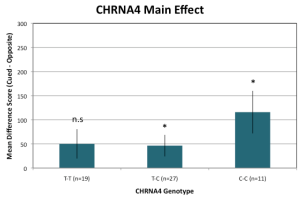
Faster and **more likely** to respond to targets appearing in the **non-cued** location when the delay is **long**.

Reaction Time: Average latency to look at targets in opposite location, subtracted from average latency to look at targets in cued location.

Difference Score = 0 – no RT benefit for targets in cued or opposite locations.

Difference Score > 0 – RT benefit for targets in opposite location **(IOR effect)**.

Results: CHRNA4 and COMT

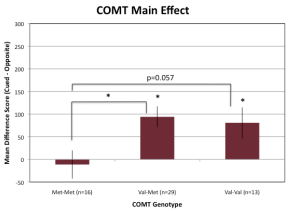


CHRNA4 Genotype

- **T-C and C-C polymorphisms show a significant IOR effect.**
- **T-T polymorphism does not show an IOR effect.**

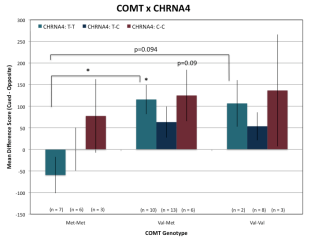
COMT Genotype

- **Val-Met and Val-Val polymorphisms show a significant IOR effect.**
- **Met-Met polymorphism does not show an IOR effect.**
- **IOR scores are higher for Val-Met and Val-Val groups compared to the Met-Met group.**



CHRNA4 x COMT Interaction

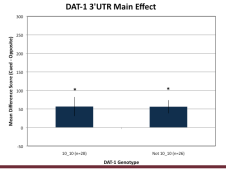
- **Effects of CHRNA4 polymorphisms are modulated by COMT polymorphisms:**



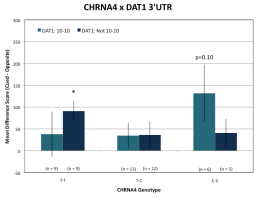
- T-C and C-C CHRNA4 polymorphisms show IOR effects **EXCEPT** in combination with the COMT Met-Met genotype.
- Significant increase in IOR scores for the CHRNA4 T-T group when also in the COMT Val-Met or Val-Val group.
- COMT main effect evident; may have stronger impact that CHRNA4.

Results: DAT 1 3'UTR

- **Both the 10/10 and non- 10/10 groups show significant IOR effects.**
- **There is no difference in IOR scores between these groups.**



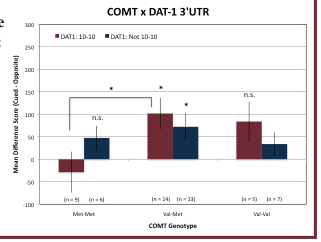
CHRNA4 x DAT1 3'UTR Interaction



- **Effects of CHRNA4 polymorphisms are modulated by DAT-1 polymorphism:**
  - The CHRNA4 T-T group showed an IOR effect **ONLY** if they also had a non-10/10 DAT1 polymorphism.
  - Infants in the CHRNA4 C-C group showed a trend for an IOR effect **ONLY** if they also had the 10/10 DAT1 polymorphism.

COMT x DAT-1 3'UTR Interaction

- **Effects of COMT polymorphisms are modulated by DAT-1 polymorphism:**
  - The COMT Val-Met group showed a significant IOR effect regardless of DAT-1 variant.
  - The COMT Val-Met group had higher IOR scores than the Met-Met group, **ONLY** if they also had the DAT-1 10/10 variant.



Discussion

Hypothesized functions of CHRNA4, COMT, & DAT-1 VNTR variants:

- CHRNA4 & DAT1 are highly expressed in parietal cortex, which is critical for IOR effect. COMT is highly expressed in prefrontal cortex (PFC).
  - CHRNA4 – C allele has been related to increased benefit from spatial cues (Bellgrove et al., 2008).
  - COMT – Val allele is associated with lower levels of DA in PFC and relatively poor performance on executive attention tasks.
  - DAT-1 – 10-10 genotype is linked to higher levels of synaptic DA and slower orienting after invalid spatial cues (Bellgrove et al., 2007).

Present Study:

- **Variation in infants' sensitivity to spatial cues likely reflects genetic influences on both reflexive orienting AND executive attention skills.**
  - CHRNA4 – C allele associated with significant/stronger IOR effects.
  - COMT – Val allele associated with significant/stronger IOR effects, perhaps due to reduced attentional control over reflexive orienting.
  - The DAT-1 VNTR affects infants' performance on the spatial cueing task **ONLY** in conjunction with the CHRNA4 or COMT polymorphisms.

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