

Research article

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Assessing the molecular genetics of attention networks

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Abstract

Background: Current efforts to study the genetic underpinnings of higher brain functions have been lacking appropriate phenotypes to describe cognition. One of the problems is that many cognitive concepts for which there is a single word (e.g. attention) have been shown to be related to several anatomical networks. Recently, we have developed an Attention Network Test (ANT) that provides a separate measure for each of three anatomically defined attention networks.

Results: In this study we have measured the efficiency of neural networks related to aspects of attention using the ANT in a population of 200 adult subjects. We then examined genetic polymorphisms in four candidate genes (DRD4, DAT, COMT and MAOA) that have been shown to contribute to the risk of developing various psychiatric disorders where attention is disrupted. We find modest associations of several polymorphisms with the efficiency of executive attention but not with overall performance measures such as reaction time.

Conclusions: These results suggest that genetic variation may underlie inter-subject variation in the efficiency of executive attention. This study also shows that genetic influences on executive attention may be specific to certain anatomical networks rather than affecting performance in a global or non-specific manner. Lastly, this study further validates the ANT as an endophenotypic assay suitable for assessing how genes influence certain anatomical networks that may be disrupted in various psychiatric disorders.

Background

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Table 1: Summary ANT values for large mixed population of normal subjects Summary means and standard deviations of attention network scores (ms) and overall reaction time.

Alerting	Orienting	Executive	Reaction Time
36 ± 22	55 ± 27	95 ± 43	540 ± 86

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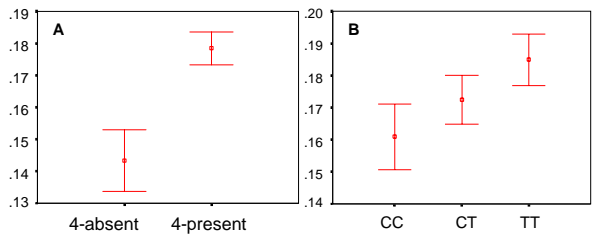


Figure 1
DRD4 and executive attention The Y-axis shows normalized executive attention scores (mean ± SE). The X-axis shows distributions for each genotypic class. Panel A shows the distribution of executive attention score as a function of exon III VNTR genotype in the 4-repeat absent vs. 4-repeat present groups. Panel B shows distribution of executive attention score as a function of a single nucleotide genotype (CC, CT and TT) at position -521.

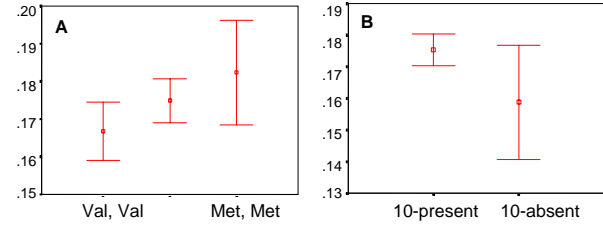


Figure 2
COMT and DAT1 and executive attention Distributions of COMT and DAT1 genotypes vs. executive attention score. The Y-axis shows normalized executive attention scores (mean + SE). The X-axis shows the distribution for each genotypic class. Panel A shows the executive attention scores for each genotypic class at the COMT Valine 108/158 Methionine polymorphism. Panel B shows the relationship between normalized executive attention scores and genotypes at the DAT1 3' UTR repeat polymorphism.

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Comparison of 'high' vs. 'low' dopamine alleles

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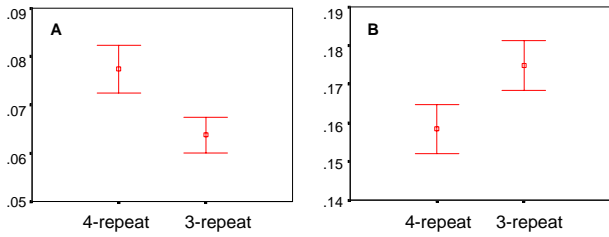


Figure 3
MAOA and alerting and executive attention Distributions of MAOA-LPR genotypes vs. alerting (Panel A) and executive attention (Panel B) scores. The Y-axis shows normalized alerting or executive attention scores (mean + SE). The X-axis shows the distribution for each genotypic class at the repeat polymorphism in the promoter of MAOA. Genotypic classes are a combination of males and females however only homozygous females were chosen, given the random nature of X-chromosome inactivation.

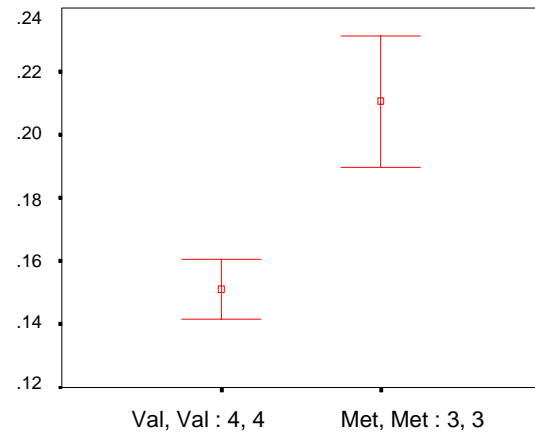


Figure 4
Effect of 'high' vs. 'low' dopamine alleles on executive attention Comparison of normalized executive attention scores in genotypic classes expected to show high and low levels of dopamine. The Y-axis shows normalized executive attention scores (mean + SE). From the entire population, 30 subjects carried the COMT (Val, Val) and MAOA-LPR (4-repeat, 4-repeat) genotypes and are expected to have relatively lower dopamine levels than 20 subjects who carried the COMT (Met, Met) and MAOA-LPR (3-repeat, 3-repeat) genotypes. These distributions are referred to as 'low' dopamine and 'high' dopamine and are shown above.

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Discussion

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Recommendations for molecular genetic studies on the ANT

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Conclusions

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Calculation of attention network efficiencies

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Methods

Subjects

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Genetic sample collection and genotyping methods

Behavioral data

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Statistical analysis of genetic vs. behavioral variation

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Authors' contributions

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