Functional MRI during performance of the Stroop task in monozygotic twins concordant or discordant for attention / hyperactivity problems

[1,2]D. van 't Ent, [3]H. Lehn, [1]E.M. Derks, [1,4]J.J. Hudziak, [1]N.M. Van Strien, [5]D.J. Veltman, [1]E.J.C. De Geus, [6]R.D. Todd, [1]D.I. Boomsma,

[1]Department of Biological Psychology, Vrije Universiteit, Amsterdam, The Netherlands
[2]Center for Neurogenomics and Cognitive Research (CNCR)
[3]Department of Circulation & medical imaging, Norwegian University of Science and Technology, Trondheim, Norway
[4]Department of Psychiatry, University of Vermont, Burlington, VT, USA
[5]Department of Psychiatry, Vrije Universiteit medical center, Amsterdam, The Netherlands
[6]Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA

Introduction

To distinguish between the genetic and environmental neurobiology of ADHD we measured fMRI during performance of the Stroop selective attention task in monozygotic (MZ) twins selected from the Netherlands Twin Register to be highly concordant or highly discordant for parental ratings on the Child Behavior Checklist Attention/hyperactivity Problem scale (CBCL-AP).

A: the contribution of genetic factors was studied by comparing fMRI BOLD activations of MZ twin pairs who scored AP concordant high with pairs in which both twins scored AP concordant low.

Attention/hyperactivity problems are highly heritable, thus differences in brain activation between these groups are likely of genetic origin.

B: environmental influences were assessed by comparing brain activations of discordant MZ pairs in which one twin scored AP high and the other AP low. MZ twins are genetically identical, within pair discordance for attention/hyperactivity is likely to arise from different environmental exposure.

Methods

fMRI was measured in 3 concordant high (3 F; 15.4 ± 2.6 yrs) , 10 concordant low (6M/4F; 15.4 ± 1.0 yrs) and 5 discordant (2M/3F; 15.0 ± 2.0 yrs) MZ twin pairs during performance of the Stroop task which involves responding to the ink color of written color words. Functional images were acquired on a 1.5 T MR system and analysed using SPM2 (Wellcome Department of Imaging Neuroscience, London, UK).

Results

Task performance

Stroop incongruent (e.g., responding red to "blue") versus congruent (e.g., responding red to "red") color-word interference across groups [reaction times (ms): 577.8 ± 118.4 vs. 536.8 ± 93.3: F(35,1) = 23.39, p < 0.001; response errors: 3.1 ± 2.1 vs. 2.3 ± 2.0: F(35,1) = 3.76, p = 0.061] was comparable between concordant high and low and discordant high and low twins.

fMRI

A: Main effect of Stroop interference (Fig. 1)

Overall, incongruent color words led to higher fMRI-BOLD activation than congruent words in the SMA (area labeled A), dorsolateral prefrontal cortices (B,C), left caudate head (D), occipital (E,F) and parietal (G,H) lobes and left cerebellum (I); reflecting the additional cognitive requirement to inhibit distracting word meaning information.

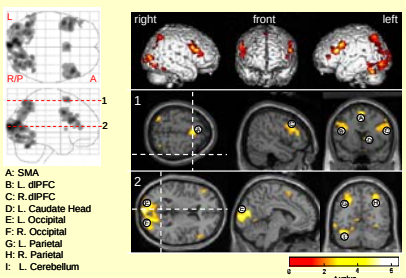

Fig. 1: Parametric *t* maps, projected on MR sections, showing clusters of increased fMRI activation after incongruent vs. congruent Stroop color-word stimuli [voxel p-value threshold p < 0.05; False Discovery Rate corrected, with minimal cluster size of 20 voxels].

B: Genetic contrast: Stroop interference for *AP high* versus *low* concordants (fig. 2)

Compared to concordant low twins, concordant AP high twins showed reduced activation to trials with high interference in left and right pre/postcentral (A,B) and medial frontal (C,D) regions, left occipital (E) and temporal (F) cortex, and right superior parietal cortex (G) and right fusiform gyrus (H).

Relatively increased activation during high interference for concordant high twins was noted in a left inferior frontal (I) and right dorsolateral prefrontal (J) region and the right caudate nucleus (K).

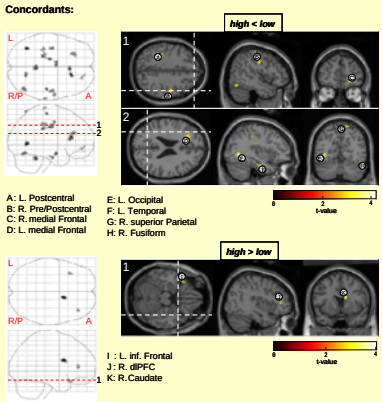

Fig. 2: Clusters indicating differences in the amount of fMRI-BOLD increase after incongruent versus congruent color-word stimuli between concordant AP high and AP low MZ twin pairs [voxel p-value threshold p < 0.01; uncorrected; minimal cluster size 10 voxels].

C: Environment contrast: Stroop interference for AP *high* versus *low* discordants (fig. 3)

Relative to their low AP co-twins, AP high discordant twins showed clusters of reduced activation to trials with high interference in the cerebellum (A,F), left dorsolateral prefrontal cortex (B,D), left and right midtemporal regions (C,G), SMA (E) and right occipital cortex (H). Increased BOLD responses with high interference were noted in right parietal/occipital cortices (I,K), left precentral (L) and left temporal (M) region, right frontal cortex (J), left- and right amygdalae (N,O) and left caudate head (P)

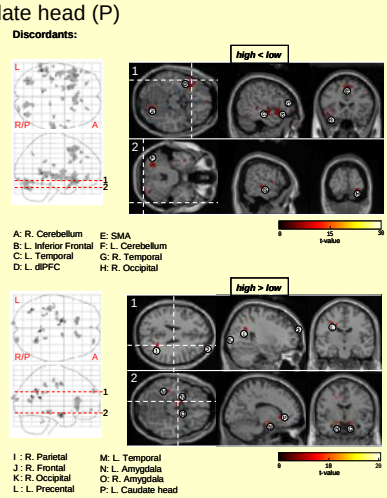

Fig. 3: Clusters indicating differences in the amount of fMRI-BOLD increase after incongruent versus congruent color-word stimuli between discordant AP high and AP low MZ twins. [voxel p-value threshold p < 0.01, uncorrected; minimal cluster size 10 voxels].

Conclusions

In agreement with earlier fMRI studies in ADHD (e.g., Zang et al., Brain Dev. 2005 Dec; 27(8):544-50) our study demonstrates increments as well as decrements in the amount of BOLD signal increase during inhibition of distracting information, that are related to parent reports of inattention and hyperactivity symptoms. Of particular interest was the finding that both concordant and discordant AP high twins showed relatively increased caudate activation while discordant AP high twins in addition showed increased amygdala activation. These findings possibly reflect a higher effort for AP high twins to achieve similar behavioral performance as AP low twins. Because the brain areas of activation differences in inattention/hyperactivity of 'genetic (high versus low concordant MZ pairs)' versus 'non-genetic (high-low discordant MZ pairs)' origin were generally distinct, we conclude that genetic and environmental risk factors for attention/hyperactivity problems may, partly, act on different brain structures.