Neuroscience Campus Amsterdam

Neuroimaging of response interference in twins concordant or discordant for inattention and hyperactivity symptoms

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

[1]Dept Biological Psychology, Vrije Universiteit, Amsterdam; [2]Neuroscience Campus Amsterdam; [3]Rudolf Magnus Institute of Neuroscience, Department of Psychiatry, University Medical Center Utrecht; [4]Dept Psychiatry, University of Vermont, Burlington; [5]Departments of Psychiatry, VU Medical Center and University of Amsterdam Academic Medical Center, Amsterdam; [6]Dept Psychiatry, Washington University School of Medicine, St. Louis.

Introduction

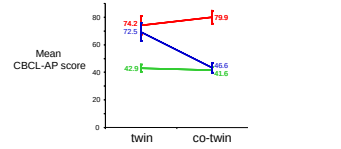
ADHD is highly influenced by genetic factors, but environmental risks are also considered important. To distinguish between functional brain changes underlying primarily genetically and environmentally mediated ADHD, we used fMRI to compare response interference in monozygotic (MZ) twins highly concordant or discordant for attention problems (AP).

- the contribution of genetic risk was studied by comparing fMRI activations of MZ twin pairs who scored AP concordant high with pairs that scored AP concordant low. Since attention problems are highly heritable, differences in brain activation between these groups are likely of genetic origin.

- the contribution of environmental risks was assessed by comparing fMRI of discordant MZ pairs in which one twin scored AP high and the other AP low. Since MZ twins are genetically identical, discordance for AP is likely due to different environmental exposure.

Methods

Participants (fig. 1): subjects were 15 years old MZ Twins from the Netherlands Twin Register, selected based on extreme scores on the Child Behavior Check List/4-18 attention problem scale, completed by the mother at 7, 10 and 12 years.



Concordant high: N=8 pairs (6F/2M) 15.4 ±1.6 Yrs
Concordant low: N=10 pairs (4F/6M) 15.4 ±1.3 Yrs
Discordant: N=9 pairs (7F/2M) 14.8 ±1.5 Yrs

Fig. 1

Tasks (fig. 2): fMRI was measured, at 1.5 T, during two tasks that probe selective attention and inhibitory control; the Stroop task and an arrow flanker task. The data were analysed using SPM5.

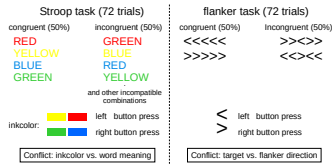


Fig. 2

Results

Task performance: We found classical effects of response interference on reaction times and response accuracy for both the Stroop and flanker task. Enhanced interference associated with high CBCL-AP scores was found only for the flanker task in the concordant twin comparison [negative effect of interference on response accuracy: -4.17 ± 4.09 (high) vs. -2.71 ± 2.32 (low), p=0.025]

fMRI: main effects (fig. 3): The fMRI main effects, across all subjects (54 twins), indicated that highly similar brain processes were active during Stroop and flanker task performance; for congruent and incongruent stimulus trials, separately, as well as for enhanced activation to response interference assessed from the 'interference: (incongruent-congruent)' contrast.

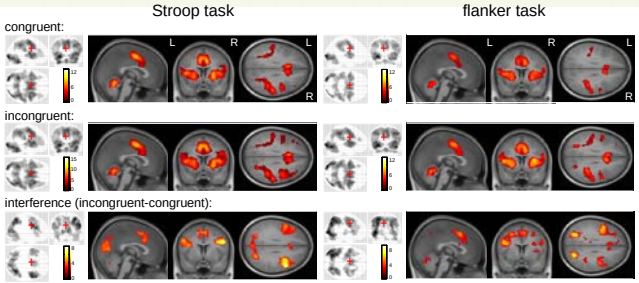


Fig. 3 voxel threshold: p < 0.05 FDR corrected.

AP related differences for the interference contrast (fig. 4)

Genetic risk: AP high vs. low twins from concordant pairs

Decreased activation to interference in AP high, compared to AP low, twins from concordant pairs was found in the left dorsolateral prefrontal cortex for the Stroop task and right parietal cortex for the flanker task.

Increased activation in AP high twins was found in the left thalamus for the Stroop and left premotor cortex for the flanker task.

Environmental risk: AP high vs. low twins from discordant pairs

Decreased activation to interference in AP high twins, compared to the AP low co-twins, from discordant pairs was found only for the Stroop task in the left and right superior temporal gyrus (STG), right fusiform gyrus and right precuneus (figure shows L. STG cluster).

Increased activation in AP high twins was found only for the flanker task in left and right premotor cortices, right middle frontal gyrus and anterior cingulate (figure shows L. premotor cluster).

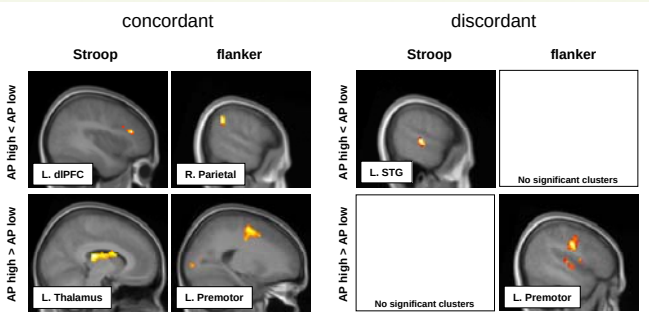


Fig. 4 voxel threshold: p < 0.001 uncorr.

Conclusions

In line with previous neuroimaging studies of ADHD, AP high twins showed decreased brain activation to response interference in frontal, parietal and temporal brain regions. Increased activation to interference in AP high twins, possibly reflecting compensatory mechanisms, was primarily restricted to premotor areas and regions associated with visual attention processing. Specific comparison of concordant twin pairs suggests that AP of genetic origin was characterized by decreased prefrontal and parietal activation, while comparison of twins from discordant pairs, suggest that AP of environmental origin was mainly characterized by decreased temporal lobe activation. These results indicate that genetic and environmental risks for attention problems affect the brain differently.

VU medisch centrum

VU University Amsterdam