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

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

1Dept Biological Psychology, Vrije Universiteit, Amsterdam; 2Neuroscience Campus Amsterdam; 3Rudolf Magnus Institute of Neuroscience, Department of Psychiatry, University Medical Center Utrecht; 4Dept Psychiatry, University of Vermont, Burlington; 5Departments of Psychiatry, VU Medical Center and University of Amsterdam Academic Medical Center, Amsterdam; 6Dept 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/18 attention problem scale, completed by the mother at 7, 10 and 12 years.

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.

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.

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 prefrontal areas and regions associated with visual attention processing. Specific comparison of discordant 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.