



Research report

Out of focus – Brain attention control deficits in adult ADHD

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ABSTRACT

Modern environments are full of information, and place high demands on the attention control mechanisms that allow the selection of information from one (focused attention) or multiple (divided attention) sources, react to changes in a given situation (stimulus-driven attention), and allocate effort according to demands (task-positive and task-negative activity). We aimed to reveal how attention deficit hyperactivity disorder (ADHD) affects the brain functions associated with these attention control processes in constantly demanding tasks. Sixteen adults with ADHD and 17 controls performed adaptive visual and auditory discrimination tasks during functional magnetic resonance imaging (fMRI). Overlapping brain activity in frontoparietal saliency and default-mode networks, as well as in the somato-motor, cerebellar, and striatal areas were observed in all participants. In the ADHD participants, we observed exclusive activity enhancement in the brain areas typically considered to be primarily involved in other attention control functions: During auditory-focused attention, we observed higher activation in the sensory cortical areas of irrelevant modality and the default-mode network (DMN). DMN activity also increased during divided attention in the ADHD group, in turn decreasing during a simple button-press task. Adding irrelevant stimulation resulted in enhanced activity in the salience network. Finally, the irrelevant distractors that capture attention in a stimulus-driven manner activated dorsal attention networks and the cerebellum. Our findings suggest that attention control deficits involve the activation of irrelevant sensory modality, problems in regulating the level of attention on demand, and may encumber top-down processing in cases of irrelevant information.

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1. Introduction

Human attention control systems have evolved to ensure rapid reaction to sudden environmental changes and to help us focus on our goals and adapt them to different circumstances (Patel et al., 2015). The skills that support attention control have probably never been as important as they are in today's modern technology society, which is filled with potentially relevant information as well as distractors (Kovach, 2010). Attention control allows us, on the one hand, to suppress irrelevant information and avoid triggering attention in a stimulus-driven manner; and on the other

hand, to selectively focus our attention on one task at a time or divide our attention between multiple tasks simultaneously. Attentional control plays an increasing role in our hectic, everyday lives. This can severely impact the quality of life for individuals with attentional control deficits, such as the 5% of the population worldwide with attention deficit hyperactivity disorder (ADHD, Polanczyk et al., 2007).

1.1. Brain networks involved in ADHD

The control of attention, which is extensively studied in healthy humans, involves widespread networks in cerebro-cortical and subcortical brain structures (Petersen and Posner, 2012, Duncan, 2013). In recent years, it has been established that the pathophysiology of ADHD involves large-scale changes that cover most brain

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areas in the attention control networks (Castellanos and Proal, 2012, Cao et al., 2014, Rubia et al., 2014). More specifically, several reviews and meta-analyses now agree that ADHD is associated with aberrant functioning of the dorsal (superior parietal lobule/intraparietal sulcus, SPL/IPS; frontal eye field, FEF) and ventral (temporoparietal junction/inferior frontal gyrus, TPJ/IFG) attention systems, the salience network (medial frontal cortex, MFC; anterior cingulate cortex, ACC; IFG, and anterior insula), the default-mode network (posterior cingulate cortex/ventromedial prefrontal cortex, PCC/VMPFC), the sensory-motor cortical areas, and the striatum and cerebellum (Dickstein et al., 2006, Cortese et al., 2012, Castellanos and Proal, 2012, Cao et al., 2014, Rubia et al., 2014). However, because the majority of recent brain imaging studies investigating the functioning of these networks in ADHD have utilized the resting-state approach, evidence of how the aberrant activity in these networks is linked to specific attention control deficits remains scarce.

1.2. Core functions of attention control

Focused attention or sustained attention that refer to selectively maintaining the focus of attention on particular stimulus features is one of the key attention control functions (e.g., Mackworth, 1968, Salmi et al., 2007). As attention is regulated by both the goal-directed or 'top-down', and stimulus-driven or 'bottom-up' function (Posner, 1980, Salmi et al., 2009, Alho et al., 2015), focusing attention typically requires suppressing the processing of irrelevant information (Sarter et al., 2001, Salmi et al., 2009, Alho et al., 2015) such as transient ambient noises that may capture attention, or more sustained background noises that require higher selectivity during the primary focus task. Attention may also be divided among multiple targets to some extent (e.g., Spelke et al., 1976; Moisa et al., 2015, Salo et al., 2017), for instance when simultaneously driving a car and speaking on the phone.

A large extent of our attentional control relates to processing auditory and visual information. Although slightly different concepts have traditionally been used in the fields of auditory and visual attention research, auditory and visual attention have many similarities. In both modalities, attention influences sensory processing at a relatively early stage, already before awareness of the stimulus (Kastner et al., 2006; Rinne et al., 2008), and there is a considerable overlap between the higher-level attention control systems in the two modalities (Shomstein and Yantis, 2006, Salmi et al., 2007, Salmi et al., 2009). Evidence spanning from neuronal pathways (Braga et al., 2017) to functional brain imaging (Salmi et al., 2007) suggests that the auditory system could be more sensitive to irrelevant information than the visual system, which in turn influence processing in a bottom-up manner (in the auditory system, bottom-up attention is often termed involuntary attention). In the visual system, bottom-up effects are typically examined in the context of exogenous orienting of attention, where an exogenous cue may facilitate the attention shift to the target location (Posner, 1980).

Although the roles of auditory and visual attention have not been examined in detail in ADHD research, each of the core attention control functions mentioned above are directly related to ADHD. Adults with ADHD have trouble maintaining sustained attention, are distracted by background noises, and have problems dividing attention among multiple tasks. This can manifest as typical inattention symptoms, such as lack of focus, absent-mindedness, and disorganized task structuring, which can hamper everyday work and academic tasks (see Barkley, 1997, see also Gawrilow et al., 2011). Developing sensitive experimental measures that capture these daily life symptoms has, however, turned out to be challenging, and it is still largely unclear which specific

cognitive brain functions are affected when individuals with ADHD perform tasks requiring these subfunctions of attention control.

1.3. Functional characteristics of attention control networks

Controlled experiments on healthy humans suggest that sensory cortical areas and ventral attention networks mediate functions that can involuntarily capture our attention in a stimulus-driven manner in both visual (Serences et al., 2005, Serences and Yantis, 2007, see also Corbetta and Shulman, 2002) and auditory (Salmi et al., 2009, Alho et al., 2015) modalities, as well as cross-modally (Yang and Mayer, 2014, Mayer et al., 2016). However, dividing attention under top-down control recruits the dorsal attention network (Johnson and Zatorre, 2006, Moisa et al., 2015; Salo et al., 2015, Salo et al., 2017), which also overlaps with the two modalities (Shomstein and Yantis, 2006, Salmi et al., 2007). Selectively focusing attention on a particular task content also activates the dorsal and ventral attention networks (e.g., Salmi et al., 2007, Serences and Yantis, 2007), but not as prominently as conditions in which the focus of attention changes (e.g., Salmi et al., 2007, Salmi et al., 2009, Alho et al., 2015). Activity in the posterior cerebellum (e.g., Salmi et al., 2007, Salmi et al., 2010; Stoodley, 2012) is often observed together with activity in the cerebro-cortical attention control networks described above. Functional coupling of the cerebral and cerebellar areas of the attention control networks is based on prominent anatomical connections, and is proposed to help optimize the related cognitive, motor, or sensory functions (see Middleton and Strick, 2000 for a review).

All complex situations involve constant dynamic interaction and competition between multiple attentional processes. Brain activation associated with different attention control functions has also been observed in largely overlapping networks (e.g., Serences and Yantis, 2007, Salmi et al., 2009, Yang and Mayer, 2014, Alho et al., 2015, Xuan et al., 2016). Hence, understanding the attention processes associated with observed brain activity requires simultaneous measurement of multiple core attention control functions and detailed cross-validation of several alternative hypotheses. Recent advances in brain imaging methods have enabled the investigation of multiple attention control processes and the relative roles of these networks within the same experiment (e.g., Salmela et al., 2016, Salo et al., 2017). This has opened up new opportunities to also study the deficits of attention control functions that manifest in widespread brain networks.

1.4. Research question and hypotheses

For the present study, we developed an experimental paradigm that allowed us to investigate the roles of focused, divided and stimulus-driven attention, as well as the effects of unimodal and bimodal visual and auditory inputs within the same experiment (Fig. 1, see Salmela et al., 2016; Salo et al., 2017). Our participants performed the auditory and visual discrimination tasks at a discrimination threshold of about 70%, i.e. at their individual performance limits. Our aim was to determine how adult ADHD affects the brain networks involved in multiple attention control functions. The included contrasts were selected on the basis of our previous studies (Salmela et al., 2016; Salo et al., 2017) which validated this paradigm among healthy participants. Previous ADHD studies have studied focused and stimulus-driven attention separately, and the neuronal correlates of divided attention have remained unclear. Our goal was, by measuring all these functions in the same study, to pursue a detailed functional characterization of the related attention deficits.

Based on previous studies on ADHD (for a meta-analysis, see Cortese et al., 2012), we expected ADHD participants to show altered activity in the dorsal and ventral attention systems,

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