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The neural basis of sustained and transient attentional control in young adults with ADHD

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ABSTRACT

Differences in neural activation during performance on an attentionally demanding Stroop task were examined between 23 young adults with ADHD carefully selected to not be co-morbid for other psychiatric disorders and 23 matched controls. A hybrid blocked/single-trial design allowed for examination of more sustained vs. more transient aspects of attentional control. Our results indicated neural dysregulation across a wide range of brain regions including those involved in overall arousal, top-down attentional control, response selection, and inhibition. Furthermore, this dysregulation was most notable in lateral regions of DLPFC for sustained attentional control and in medial areas for transient aspects of attentional control. Because of the careful selection and matching of our two groups, these results provide strong evidence that the neural systems of attentional control are dysregulated in young adults with ADHD and are similar to dysregulations seen in children and adolescents with ADHD.

1. The neural basis of sustained and transient attentional control in young adults with ADHD

Although a variety of studies have examined the neural systems dysfunctional in children with ADHD (for a review Bush, Valera, & Seidman, 2005), fewer have carefully examined the functional and anatomical abnormalities associated with ADHD in adulthood. While early positron emission tomography (PET) studies suggested the possibility of a general reduction in neural responsiveness (e.g., Zametkin et al., 1990), more recent research has implicated a variety of regions. Bush et al. (1999) suggested that underactivation of the dorsal anterior cingulate cortex (ACC), in the face of otherwise intact functioning of a fronto–striatal–insular network, underlies the inattention and impulsivity in adults with ADHD. Other research based on neuroanatomical comparisons between adults with ADHD and controls (Bush et al., 2005; Makris et al., 2007), as well as functional imaging, suggests disruption in prefrontal and parietal regions involved in executive control (Hale, Bookheimer, McGough, Phillips, & McCracken, 2007; Valera et al., 2005; Wolf et al., 2009). Both prefrontal regions involved in "cold" executive function as well as those involved in "hot" emotional functions (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006) have been implicated. And still other recent research suggests potential dysfunction of the "default" brain network (Buckner, Andrews-Hanna, & Schacter, 2008) both in terms of reduced coherence of activity (Uddin et al., 2008) as well as specific disruptions of this network in relation to regions involved in cognitive control such as the anterior cingulate (Castellanos et al., 2008). Given these inconsistencies, and the overall dearth of functional neuroimaging studies in adults with ADHD, we believe that additional studies are warranted.

The focus of the current study was to compare brain activation during performance of an attentionally demanding task for a well-characterized college-aged sample of young adults with ADHD who were not comorbid for other psychiatric disorders or learning disabilities and controls similar in IQ and age. Such careful sample selection was designed to maximize the possibility that any group differences were likely attributable to ADHD rather than other factors, such as co-morbid psychiatric disorders or overall level of intelligence. We utilized the Stroop task, not only because it is considered the "gold standard" of attentional tasks (MacLeod, 1991) but also because our prior neuroimaging studies in neurologically normal young adults performing this task (Banich et al., 2000a,b; Liu, Banich, Jacobson, & Tanabe, 2004; Liu, Banich, Jacobson, & Tanabe, 2006; Milham & Banich, 2005; Milham, Banich, & Barad, 2003; Milham, Banich, Claus, & Cohen, 2003; Milham et al., 2001) provides

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a strong empirical and theoretical base from which to interpret any observed group differences.

Because our prior research suggests distinct roles for medial vs. lateral prefrontal regions involved in attentional control, we wished to investigate whether one or both of these systems are affected in young adults with ADHD. Our prior neuroimaging work indicates that the dorsolateral prefrontal cortex (DLPFC) is very important in implementing a top-down attentional bias or “goal state”, especially one that must be maintained over time in a sustained manner (e.g., Banich et al., 2000a; Milham, Banich, & Barad, 2003; Milham, Banich, Claus, et al., 2003). Because a major symptom of ADHD is distractibility and an inability to stay on task, we hypothesized that this region might function atypically in young adults with ADHD. Our prior results also suggest that caudal regions of the dorsal anterior cingulate (BA 32) are more involved in response-related aspects of attentional control that varies in a more transient (i.e., trial-by-trial) manner and that such control is dissociable from that exerted by DLPFC (e.g., Milham, Banich, & Barad, 2003; Milham, Banich, Claus, et al., 2003; Milham et al., 2001, 2002). Given prior research that suggests moment-to-moment fluctuations in cognitive control, at least in children with ADHD (van Meel, Heslenfeld, Oosterlaan, & Sergeant, 2007), we also wished to investigate the integrity of functioning of these medial prefrontal regions in adults with ADHD.

To distinguish between sustained and transient aspects of cognitive control, we employed a hybrid blocked-event related design (Visscher et al., 2003). Blocked activity provides a rough index of the ability to sustain attentional control, while event-related activity provides an index of transient control. Participants were required to manually identify the ink color in which words were presented. Our design included three different types of blocks that varied by the type of word that was presented: incongruent (e.g., “red” in blue ink), congruent (e.g., “red” in red ink), and neutral (e.g., “sum” in red ink) blocks. For all three blocks, one must maintain an attentional set towards ink color identification and avoid the more automatic process of word reading. However, the blocks vary in the degree to which the stimuli themselves serve as a reminder of or reinforce the required attentional set (i.e., to pay attention to ink color). As argued by Kane and Engle (2003), the conflict inherent in the incongruent word reminds one that word reading is distracting and not task relevant (“Let’s see, the ink color is red, the word is blue. Now which one of these is important?”), but is lacking on congruent trials where simply reading the word can substitute for correctly identifying ink color. Hence, if the neural substrate for maintaining a top-down set is dysfunctional in young adults with ADHD, one would predict atypical activation of DLPFC compared to controls for all three blocks (as compared to a fixation baseline). Furthermore, this effect should be greatest for the congruent blocks in which the attentional set is not reinforced by the stimuli themselves and least for the incongruent blocks where the task inherently reminds one of the attentional set to be maintained.

To examine transient changes in attentional control, we varied trial types within block (e.g., Milham et al., 2001 for a similar approach). Half of the trials within each block were neutral and identical across all blocks (these we refer to as neutral frequent trials) while the remainder of trials were specific to that block (e.g., congruent, incongruent, neutral infrequent). Thus, within a given block, attentional demand on a trial-by-trial basis was unpredictable. In all cases, the block-specific trials (incongruent, congruent, and neutral infrequent) engendered higher attentional demand than the neutral frequent trials, which provide a common baseline against which to evaluate transient aspects of attentional control. Incongruent trials are attentionally demanding because there are two conflicting sources of color information, congruent trials are demanding because they require one to differentiate whether the ink color contained in the word or that contained in the ink color should be used to guide responding (see Milham & Banich, 2005; Posner, DiGiralomo, & Parasuraman, 1998 for a longer discussion), and neutral infrequent trials because words presented less frequently capture attention (see Milham, Banich, & Barad, 2003; Milham, Banich, Claus, et al., 2003). Our prior work indicates that caudal regions of dorsal ACC are important in processing transient aspects of attentional control that cannot be subsumed under a general attentional set for task-relevant processes (e.g., Milham, Banich, & Barad, 2003; Milham, Banich, Claus, et al., 2003). Hence, if this neural substrate for transient attentional control is also disregulated in adults with ADHD, one would predict atypical activation of medial prefrontal regions, including caudal regions of dorsal ACC.

2. Method

2.1. Participants and recruitment

2.1.1. Participants and recruitment procedures

Study participants consisted of 23 adults who met criteria for DSM-IV ADHD combined subtype (9 female, 14 male) and a control group of 23 participants without ADHD (10 female, 13 male). A three-stage screening procedure was used to identify the final groups.

2.2. Initial screening of the unselected sample

An unselected sample of 3913 undergraduates completed a battery of self-report rating scales that included the Self-Report form of the *ADHD Current and Childhood Symptom Scales* (Barkley & Murphy, 1998). The initial screening measures were administered to groups of 20–40 individuals as part of the research participation requirement of a large introductory psychology course. Permission was also requested to allow us to send the *Other Report* version of the *Current and Childhood Symptom Scales* (Barkley & Murphy, 1998) to the participant's parent or other primary caregiver during childhood. Approximately 72% of the participants provided consent for the questionnaire to be sent to their parent or caregiver.

2.3. Individual assessment of groups with and without DSM-IV ADHD

As part of an ongoing study of neuropsychological functioning in young adults with ADHD, a subset of participants from the initial screening sample were invited to participate in a more extensive individual testing session that included measures of general intelligence, academic achievement, and neuropsychological functioning. This subset included participants who met symptom criteria for any DSM-IV ADHD subtype based on parent or self-report ratings on the *Childhood and Current Symptom Scales*. They were invited to complete the individual testing session ($N = 207$) as were a randomly selected comparison sample without ADHD ($N = 98$).

2.4. Identification of groups with and without DSM-IV ADHD combined type for the current fMRI study

2.4.1. Diagnostic algorithm for the combined type

At the conclusion of the individual assessment session, participants who met criteria for DSM-IV ADHD-combined type and who met all inclusion criteria for the MR protocol were invited to participate in the current fMRI study ($N = 23$). Because the diagnosis of the combined type in adulthood is complicated by the fact that symptoms of ADHD decline with increasing age, particularly on measures of hyperactivity–impulsivity (e.g., DuPaul et al., 1998; Nolan, Volpe, Gadow, & Sprafkin, 1999; Nolan, Gadow, & Sprafkin, 2001), we used the follow four criteria: (1) Retrospective reports by the participant or the parent indicating that he or she met DSM-IV criteria for the combined type during childhood; (2) the participant either currently met criteria for DSM-IV ADHD ($N = 20$) or scored above the 90th percentile on the ADHD symptom measures while exhibiting marked functional impairment, consistent with the *DSM-IV* specification of *ADHD in partial remission* ($N = 3$); (3) the ADHD symptoms led to significant functional impairment, and (4) the onset of the ADHD symptoms was prior to 12 years of age. This age threshold was used rather than age 7 because prior studies suggest it is more reliable and valid than the threshold specified in DSM-IV (e.g., Barkley & Biederman, 1997; Nigg et al., 2005).

2.4.2. Treatment history

Of the 23 individuals in the ADHD group, 22 had received a previous diagnosis of ADHD. Twenty individuals had been prescribed psychostimulant medication during their lifetime, and 14 individuals had a current prescription for mixed amphetamine salts (*Adderall XR*; $N = 9$), methylphenidate (*Concerta*, $N = 3$; *Ritalin*, $N = 1$), or dexmethylphenidate (*Focalin*, $N = 1$). Participants with a current prescription for stimulant medication agreed to refrain from taking the medication for 24 h prior to their participation in the study. One participant with a current prescription for a nonstimulant medication (bupropion, *Wellbutrin*) was not asked to discontinue the medication.