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# Inattentiveness in attention-deficit/hyperactivity disorder

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## Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder with a long-term impact on functioning, productivity and quality of life of patients. This impact is largely due to the symptoms of inattentiveness. However, despite its impairing role in the lives of ADHD patients, inattentiveness has been studied relatively less frequently than have symptoms of impulsivity/hyperactivity and problems with executive function. This review therefore seeks to integrate the neuropsychological theories and current findings in the research fields of neuropsychology, neurophysiology, and neuroimaging, in an attempt to gain a more complete understanding of the role that inattentiveness plays in ADHD, as well as to suggest directions for future studies. The need for a more comprehensive understanding of inattentiveness and ADHD, which integrates findings from each of the three disciplines mentioned above, is emphasized.

### Keywords

attention-deficit/hyperactivity disorder; inattentiveness; brain pathways; neuropathology

## Introduction

Attention-deficit/hyperactivity disorder (ADHD), which is identified in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)[1], is the most commonly-diagnosed neurodevelopmental disorder of childhood. Its high prevalence (~3–5% in



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children worldwide, with a high male-to-female ratio[2]) makes it an area of tremendous concern for parents, teachers and researchers alike. Symptoms of ADHD have been reported across all racial and socio-economic groups[2]. Additionally, although, in part due to its childhood onset, it is traditionally considered as a childhood disorder, more recent research findings suggest that the impairments associated with ADHD often extend into adulthood and can cause life-long effects on cognitive and social functioning[3,4]. The cost of ADHD also makes it a priority for interventional research. In the United States, for example, individuals with ADHD have been found to experience 4% higher costs related to declines in workplace productivity and 44% greater health care costs each year[5].

According to the DSM-IV, diagnosis of ADHD is based upon symptoms of either of the two different areas or both, inattentiveness and hyperactivity/impulsivity (Table 1)[1]. However, the neurobiological foundation of the inattentiveness component has yet to be fully explored[6]. Here, we review and summarize the neuropsychological, neurophysiological and neuroimaging findings on the inattentiveness that is associated with the disorder, in an attempt to advance scientific understanding of this inattention.

## Neuropsychological Studies

It is currently difficult to compare the neuropsychological findings from ADHD because there still lacks a common definition and theory of the disorder. For example, the Cognitive-Energetic Model views the executive system as controlling effort, arousal and activation[7,8]. In turn, these are thought to modulate the mechanisms of encoding, stimulisearching, decision-making and motor organization[9]. In contrast, other models propose that attention is comprised of at least three areas (automatic orienting, voluntary orienting and vigilance/alerting) or is controlled by either or both of the top-down and bottom-up attentional processes[9,10].

While the exact model by which attention works is unclear, several areas are generally recognized: executive attention (also called selective attention), orienting attention, alerting, shifting attention (also referred to as set-shifting) and sustained attention (also known as vigilance)[11–13]. These are not uniformly labeled in the literature. However, the conceptualization of each aspect of attention is generally consistent. While the precise areas of attention that play a role in ADHD remains uncertain, it seems that executive and alerting attention are the most frequently implicated in the literature on ADHD[11,13].

It is not surprising that children with ADHD have problems with executive attention since difficulty in filtering stimuli would logically result in inattention[14,15]. Deficits in alerting attention, though less frequently studied, have also been found in individuals with ADHD in such a way that they are significantly less aroused in response to stimuli and experience difficulty processing information in highly alert states[14]. In contrast, orienting attention which involves determination of what to be attended, has been shown to be largely not problematic for individuals with ADHD[13,14]. It seems therefore, that individuals with ADHD can identify relevant stimuli similarly to those without the disorder, but are less aroused and have difficulty figuring out the distractors. This may be particularly true when they are highly alert. As for the shifting attention, the role it plays in ADHD remains

unclear. Some studies counterintuitively indicate that the ability to switch attention sets is enhanced in spontaneously hypertensive rats (SHR) (a mutant rat strain that serves as a model of the hyperactive, impulsive and inattentive behaviors associated with ADHD)[16]. However, this has not been replicated in humans and shifting attention is not a useful measure in the identification of ADHD[6], despite some findings to the contrary[15,17,18]. Lastly, sustained attention, despite its historical role in the identification of ADHD, has not been found to be consistently impaired in individuals with ADHD[13,19].

More recently, theories of attention have begun to consider the findings of increased intraindividual variability (IIV) across tasks in individuals with ADHD[20,21]. IIV has been measured in several areas of functioning in individuals with ADHD, such as attention processes in general education classrooms[22], as wells as speed, variability, and timing of motor output[23]. However, most commonly it is associated with IIV in reaction times (RTs). Several theoretical explanations exist for the prevalence of IIV in RTs in ADHD. These include problems with maintaining attention, deficient motivation, and default-mode network interference (discussed later). Interestingly, individuals with ADHD are found to have decreased IIV in RTs when a task is fast-paced or involves a reward[20]. Although IIV alone does not present a complete theoretical explanation for inattention in ADHD, it certainly presents interesting information about attentiveness[20].

Another prominent theory of ADHD considers symptoms of the disorder, including attention deficits, to be related to a breakdown in executive function[24,25]. The concept of executive function is more comprehensive than that of executive attention. In addition to the overall attention processes involved in the later, executive function also includes inhibition, shifting attention, planning and working memory[26]. In fact, as Goulden and Silver noted, executive functioning is multifaceted and is therefore neither easily defined nor measured[27]. Wolf *et al*. best approximated a description of executive function by stating that it is the entity that governs the cognitive domains that relate to the control of thinking and problem-solving[28]. Also, it has been noted that the specific cognitive activities impacted by executive functioning are those that concern the pursuit of a goal[27]. When those areas of executive function associated with attention are measured, decreased scores are found in individuals with ADHD. Similarly, in a young adult follow-up study, ADHD group made significantly more inhibition errors and showed slower RTs compared to the control group[24]. As was previously noted, RTs are thought to be related to adequate maintenance of attention[20].

In short, although the precise ways in which attention is impaired in ADHD remain unclear, several areas of inattention are quite evident in individuals with ADHD. Inattentiveness is associated with the long-term educational achievement, learning problems, and scores on intelligence tests and quality of life[29–32], and is therefore a key component of the disorder.

## Neurophysiological Studies

Animal models of ADHD provide a glimpse of the neurological underpinnings of the disorder. To date, SHRs have been the most commonly investigated animal model and studies have found links between ADHD-like behaviors and impaired dopamine release in the prefrontal cortex, nucleus accumbens and striatum[33]. The locus coeruleus-

norepinephrine system, which is thought to be responsible for optimizing arousal and facilitating sustained attention, is also impaired in SHRs, supporting the theory that inattention in ADHD is related to hypoarousal and problems with alerting attention[14,34,35].

In an effort to identify brain areas and networks that play a role in the ADHD-associated inattentiveness, event-related potentials (ERPs) were used to measure brain activity in response to specific stimuli. These responses are thought to reflect various aspects of cognition, including attention[34]. Like studies of SHRs, ERP studies on humans with ADHD have also found evidence of dysregulation of the locus coeruleus-norepinephrine system[34,37–39]. However, these findings should be viewed cautiously, since they are largely based on differences in P3 amplitudes, which is thought to indicate attentiveness to a stimulus but may be moderated by intelligence and age[36,40,41]. Thus, the role that the locus coeruleus-norepinephrine system plays in the symptoms of inattention remains uncertain. However, studies of P3 amplitudes offer other areas of investigation. For example, as early as 1986, variations in P3 amplitudes in response to auditory stimuli were identified and thought to be related to inefficient allocation of attention[42]. A more recent study using a visual two-choice RT task found a delayed peak latency of early anterior ERPs (N1, P1, N2), a larger effect of stimulus type on the frontal negativity (N530) and the posterior late negativity (nSW), and a smaller effect on anterior N2 and posterior P3b amplitude in ADHD children, with no difference in RT (probably due to the large between-subject RT variability) or correct responses in performance between ADHD and control children[43]. This discrepancy between performance and P3 amplitude results indicates that individuals with ADHD compensate for some of their attention deficits using frontal brain regions[43]. Other ERP findings examined inhibition in response to stimuli. For example, several studies have found problems with both the inhibition of responses to non-stimuli and difficulties in orienting attention toward a particular task[44–46].

Electroencephalogram (EEG), which uses externally placed electrodes to measure electrical activity within the brain, indicates abnormal biological processes when distorted activity is displayed[47]. One important EEG finding of ADHD is the decreased inhibition of default-mode network activity in ADHD, as indicated by abnormality of very-low-frequency brain activity[48–50]. The default-mode network consists of spontaneous activity that occurs in various areas of the brain during resting state. This activity decreases when individuals engage in tasks that require attention[51]. Thus, it has been theorized that some of the inattention associated with ADHD may be the result of a failure to inhibit processes that are active during normal periods of inattentiveness and rest[52]. In addition, EEG studies have revealed abnormalities of the delta and alpha wave patterns in individuals with ADHD[53]. Alterations in delta wave patterns appear to reflect a decrease in brain maturation and problems with attention to task, while variations in the amount of alpha wave activity during resting states and attention tasks suggest inefficient brain processing[53,54]. However, the pattern of increased theta and slowed alpha activity is not a unique feature in ADHD. This has also been identified in several other disorders, including learning disorders, obsessive compulsive disorder and some dementias. Thus, while increased theta and slowed alpha activity may be related to the symptoms of ADHD, this pattern is certainly not limited to individuals with ADHD[55].

Magnetoencephalography (MEG) measures the spatial and temporal aspects of brain activity. As a result, studies frequently use both ERP and MEG to evaluate the activity in a specific brain region in response to an event[56]. Studies have found impairments in various areas associated with attention in individuals with ADHD. For example, the ventral attentional networks appear to be deficient in situations that require switching attention from one stimulus to another[38]. In fact, abnormal activation patterns have been found in some specific brain regions of individuals with ADHD during attentional shifts. Of particular interest are the diminishing of medial temporal lobe and the later left anterior cingulate cortex activation, and early activity in posterior superior temporal gyrus and the inferior parietal lobule which are rarely activated in control children, in response to set-shifting cues[57]. These findings provide evidence that deficits in shifting attention play a role in the ADHD symptoms of inattention. However, this is curious since, as has been noted, impaired shifting attention does not appear to be a reliable behavioral marker of ADHD[15,18,58] and future research ought to investigate this discrepancy. In addition, one MEG study found in adults with ADHD significantly reduced high-frequency (14–30, 30–56, 64–82, 82–106, 124–168, and 184–228 Hz) brain activity in the default-mode network, particularly in the medial prefrontal cortex, compared with the control adults[59]. This further supports the frequent implication of the default-mode network in various studies of ADHD. More recently, in a pharmaco-MEG study using auditory stimulation, Wilson *et al.* found reduced high-frequency (40 Hz) gamma activity (which is essential to attention) in ADHD adults than in those without ADHD[60]. These MEG findings suggest diverse patterns of abnormal brain activity associated with ADHD.

## Neuroimaging Studies

Magnetic resonance imaging (MRI) studies constitute a critical part of ADHD research and greatly contribute to the scientific understanding of the associated inattentiveness. Studies that use MRI data to look at the abnormalities in the brains of patients with ADHD fall into three categories based on the types of images acquired: structural, diffusion tensor imaging (DTI) and functional (fMRI). Structural images highlight differences in the various anatomical areas of the brain, DTI reveals variations in the white matter trace flow to and from different regions, and fMRI focuses on hemodynamic activations. In general, MRI findings on ADHD have focused on two distinct areas: brain structures and connectivity among these structures.

Structural MRI studies have revealed a wealth of data on multiple brain regions that appear to be implicated in the symptoms of inattention associated with ADHD. The most often cited of these are the prefrontal, frontal and cerebellar regions[61–64]. The prefrontal region is thought to be responsible for various aspects of attention including sustained and executive attention. In addition, studies of lesions in this area have found that prefrontal damage can result in such symptoms as distractibility and poor planning[63]. Thus, it is not surprising that this brain area plays a role in the ADHD symptoms of inattention[63]. Reduced thickness of the cerebral cortices, smaller volume of the caudate nucleus, and reduced white matter in bilateral frontal regions and the cerebellum seem to be prevalent in individuals with ADHD[61,62,65,66]. Not surprisingly, DTI has also shown abnormalities in the frontal and temporal regions in brains of ADHD patients, suggesting decreased integrity of the white

matter in these individuals[67–69]. For instance, Konrad *et al.* by using DTI, detected a significant increase in the mean diffusivity (MD) in the frontal portion of the left frontooccipital fasciculusin adult ADHD patients compared with the control, and a significant negative correlation of the MD values in the left inferior longitudinal fasciculus with the attentional performance[69]. The cortico-striato-thalmo-cortical (CSTC) loop, which helps to regulate attention, emotion and cognitive processes, displays structural and functional abnormalities in ADHD. As a part of the loop, the thalamus is also involved in the problems of inattention in children with ADHD. In a recent study, Xia *et al.* found significant regional atrophy in the left thalamus, though behavioral evidence of this was not available at the time of writing[70].

Functional connectivity studies have identified several areas that seem to play a role in ADHD-associated inattention. Cao *et al.* by using seed-based correlation analyses in fMRI, revealed decreased resting-state connectivity between the putamen and both ipsi-lateral and contra-lateral brain structures and it is thought that this may contribute to attention deficits[71]. In addition, fMRI studies have replicated EEG findings that attention problems may be related to the impaired inhibition of default networks in individuals with ADHD, lending support to theories of inattention that focus on such impairment in inhibition of the default-mode network[52,72]. Furthermore, in the study by Xia *et al.*, decreased connectivity of the thalamus with the striatum and motor cortex in the left hemisphere was found in children with ADHD[70]. As previously noted, since the thalamus plays a role in both conveying sensory information and regulating arousal, it is likely that these abnormalities participate in inattentiveness[70].

Other fMRI studies have also found abnormal activitions in specific brain regions in ADHD, particularly the ventrolateral prefrontal regions and the dorsolateral prefrontal cortex. These areas are thought to be responsible for attention allocation, maintenance and shifting, and overall attention, respectively[73,74]. Additionally, these are also involved in attention networks[75]. Taken together, these findings suggest that patients with ADHD have difficulties to adequately allocate and sustain their attention. This could lend credence to the theory that inattention in ADHD is related to problems with arousal and alerting attention[14,34].

Still other findings suggest that specific neuronal networks that play a role in attention may be implicated in ADHD. For example, the frontoparietal attention network is indicated to play a significant role in selective attention[75]. Problems with this network could explain the difficulties with selective attention that are commonly cited in the literature on ADHD. Besides, impairment in the prefrontal cortical networks has been found in children with ADHD[76], and abnormal connections between these networks and other brain regions (namely, the cerebellum, striatum and parietal regions) have also been reported. Since these networks play a role in maintaining executive control of attention, such abnormalities could result in problems with executive attention[76]. In yet another study, Tomasi *et al.*[77] found poor connectivity in regions of the dorsal attention and default-mode networks and in cerebellum, and higher connectivity in reward-motivation regions. The latter also showed decreased connectivity with regions from the default-mode and dorsal attention networks in children with ADHD. This decrease in the communication between reward response and

attentional control may contribute to deficits in overall attentiveness as well as to some of the other behavioral deficits of ADHD[77].

## Conclusion

ADHD is a disorder that results in broadly impaired functioning and has a long-lasting impact on quality of life. In part, this is due to symptoms of inattentiveness. However, while a wealth of information on the pathology of ADHD has been obtained over the past decades, the cause of symptoms of inattentiveness remains uncertain, probably due to the difficulty integrating findings into a unified understanding of attention and ADHD. Current understanding of the neurobiological underpinnings of ADHD is fragmented and findings are often varied. A more integrated understanding is, therefore, essential before these findings can effectively join the behavioral and theoretical knowledge of ADHD. Until a unified conceptualization of the disorder is achieved, the impact of findings from scientific studies in this area will be limited.

Nonetheless, evidence from the fields of neurophysiology and neuroimaging has yielded new information on ADHD and inattentiveness that can eventually be linked to a theoretical understanding of the disorder. Future studies directed at implementing this linkage and developing a more comprehensive understanding of attention that integrates findings from psychology, neurophysiology, neuroimaging and other domains are required. Specifically, a major focus of work on the inattentiveness of ADHD may be the development of a better understanding of how neurological findings are related to behavioral symptoms and clinical measures of these symptoms. One way is to address the current discrepancies among findings in each of these fields. For example, determining why findings of neurophysiological abnormalities in brain regions associated with shifting attention do not translate into consistent behavioral evidence of problems with shifting attention may shed light on important connections between psychological and physiological data. An important consideration of this and all future research should be that gender may play a role in the pathophysiology of the disorder, so possible gender differences should be taken into account[70]. In addition, more research specifically targeting the symptoms of inattentiveness in ADHD is needed in each of the three disciplines addressed in this review.

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## Table 1

The symptom clusters of ADHD as specified in the DSM-IV (text revision)

| Two areas of ADHD | Symptoms |
|---|---|
| Inattention | • Inattention to detail |
| | • Careless mistakes |
| | • Difficulty sustaining attention |
| | • Failure to listen when spoken to |
| | • Failure to follow through on or finish activities |
| | • Failure to fully carryout instructions |
| | • Difficulties with organization |
| | • Avoidance of tasks that require sustained attention |
| | • Loss of important things |
| | • Distraction by external stimuli |
| | • Forgetfulness |
| Hyperactivity/Impulsivity | HYPERACTIVITY |
| | • Failure to stay still |
| | • Inability to remain seated |
| | • Difficulty controlling behaviors |
| | • Aversion to quiet play and activities |
| | • Excessive verbalizations and activity |
| | IMPULSIVITY |
| | • Failure to inhibit responses |
| | • Difficulty with turn taking |
| | • Recurrent interruptions to others |
| | • Tendency to bother others |

ADHD, Attention-deficit hyperactivity disorder; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition.