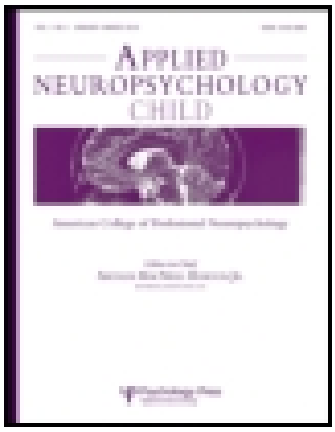

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The Role of the Thalamus in ADHD Symptomatology and Treatment

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The Role of the Thalamus in ADHD Symptomatology and Treatment

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Attention-deficit hyperactivity disorder (ADHD) is a chronic disorder with symptoms of inattention and impulsivity that partially remit with age. A review of longitudinal studies of children and adolescents with ADHD showed that the majority will have continued cognitive and functional impairments into adulthood. The thalamus likely plays a prominent role in ADHD symptomatology, based on evidence that the thalamus generates waking-state electroencephalography (EEG) rhythms along with extensive thalamic neural circuitry connections with cortical and subcortical areas. Research demonstrates a specific abnormality in the thalamic pulvinar nucleus in ADHD populations. The thalamus can also play a role in ADHD treatment, based on solid evidence that both animals and humans can learn to self-regulate EEG oscillations. Given the underarousal and sleep disturbance commonly seen in ADHD, along with data that indicate an increased dosage of ADHD medication may improve behavioral control at a cost of lowered cognitive functioning, further investigation of the role for self-regulation through EEG training is warranted.

Key words: *ADHD, attention-deficit hyperactivity disorder, child, EEG, self-regulation, thalamus*

Attention is a complex and poorly operationalized dynamic process that is better observed in its absence than in its presence. On-task behavior varies greatly according to the task demands and the arousal state of the individual, but it is the functional outcome that is the focus of clinical evaluation and recommendations. Individuals who can perform adequately on neuropsychological measures of aspects of sustained and divided attention do not always do so outside the tightly controlled and monitored conditions of an evaluation, and neither pharmacological nor cognitive-behavioral interventions have been shown to cure attention-deficit hyperactivity disorder (ADHD; Molina et al., 2009).

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The role of the thalamus is a neglected component of ADHD research and treatment options. Crucial neural circuitry connecting cortical and subcortical structures passes through the thalamus, and it has been established that the thalamus generates waking-state electroencephalography (EEG) signals (Sherman & Guillery, 2006, 2011). Therefore, thalamic involvement in arousal and motivation is likely. Common components of ADHD include underarousal and sleep disturbance, which links the thalamus with ADHD symptomatology. Finally, research dating back to the 1960s demonstrates in both animal and human studies an ability to self-regulate aspects of EEG oscillation (Howe & Sterman, 1972, 1973; Lantz & Sterman, 1988; Lucas & Sterman, 1974; Sterman, 1981, 2010; Sterman, Howe, & Macdonald, 1970; Sterman, LoPresti, & Fairchild,

1969), suggesting a role for the thalamus in ADHD treatment, through EEG-based self-regulation. This review will address the role of the thalamus in ADHD by focusing on three key areas: (a) the chronicity of ADHD; (b) the role of the thalamus in ADHD symptomatology; and (c) the role of the thalamus in ADHD treatment, while focusing on the thalamus as the generator of the EEG signal.

CHRONICITY OF ADHD

In the largest longitudinal study to date of preschoolers diagnosed with ADHD, known as the Preschool Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS), Riddle et al. (2013) provided support for the understanding that early-manifesting ADHD is a persistent condition that continues into the middle school years, regardless of the type of intervention or the age at which it was started. Nearly 90% of the 186 preschoolers diagnosed with ADHD at the beginning, middle, and end of the 6-year study continued to have significant ADHD symptoms 6 years postdiagnosis. Symptoms of inattention, hyperactivity, and impulsivity were equally severe whether or not the child took prescription medication for the condition. Approximately two thirds of the children in the study were taking medication. Significant hyperactivity and impulsivity were found in 62% of those on medication versus 58% of those taking no medication. Significant inattention was found in 65% of those on medication versus 62% of those taking no medication. Children with comorbid oppositional defiant disorder or conduct disorder were 30% more likely to have persistent ADHD symptoms compared with those who had ADHD alone.

The largest longitudinal study to date of children and adolescents with ADHD by Molina et al. (2009) showed no differences in functional outcome between common ADHD treatments. The effects of methylphenidate (Ritalin), cognitive-behavioral therapy, and combined medication and behavioral training were examined during the course of 8 years from childhood through high school graduation; results showed no differences in functional outcome of these three approaches to symptom management at the end of the study period. Those with the best outcomes had the least severe symptoms at the start of the study and responded well to one of the interventions early in the treatment. In general, those with ADHD were less likely to have a driver's license and were more likely than controls to have had some involvement with the legal system. None of those with ADHD achieved cognitive and academic outcomes comparable to the controls. Of the children who took medication, only 32% took their medication more than 50% of the time. Those assigned to either the medication or medication-plus-behavioral therapy conditions were the main participants who took medication. By the end of the study, only 32% were taking their medication, but there was no indication that they had "outgrown" their ADHD symptoms other than motor hyperactivity. There was no significant decrease in impulsiveness, although hyperactivity tended to remit over time.

The best predictors of improvement were having had less severe symptoms at ages 7 to 9 years, having had fewer conduct problems and intellectual challenges, having some social-demographic advantages, and having had any positive response to any therapeutic intervention. Again, there was no difference in outcome in any of the interventions except that after 8 years, the cohort that had continuously taken methylphenidate had better math achievement scores on the Wechsler Individual Achievement Test compared with other groups, but even the continuously medicated cohort still scored a half standard deviation lower than the control group on math achievement (Molina et al., 2009). Although there are various examples in different career fields of highly successful individuals with ADHD with and without comorbid learning disorders, the Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) study demonstrated that over time, the data do not support the notion of most individuals with ADHD "outgrowing" their ADHD to the point of not having residual functional impairments.

With respect to medication, emerging research demonstrates that methylphenidate has a narrower therapeutic window than is commonly believed. Hale et al. (2011) demonstrated a difference in the optimal dosage to control hyperactivity that was higher than that needed for optimal control of inattention and cognitive symptoms associated with ADHD. These authors hypothesized that the higher dosage needed for behavioral control may interfere with cognitive functioning that responds better to a lower dosage. This observation was recently supported and advanced when Aarts et al. (2014) used blood oxygen-level-dependent (BOLD) monitoring of patients with Parkinson's disease and normal controls during a task that enabled the measurement of task switching, reward processing, and error rates. The authors found that levodopa, a medication that increases the availability of dopamine, improved performance among 15 patients with Parkinson's disease on a switching task and increased signal in the dorsomedial striatal area. When medication was manipulated to increase the ventromedial striatal signal, reward anticipation and motivation became impaired. The authors concluded that a medication level that increased task-switching cognitive function simultaneously resulted in poorer processing of motivation for rewards. Heterogeneity in response to medication was observed depending on the individual's level of dopamine depletion.

The findings of Hale et al. (2011) are particularly relevant for pediatric neuropsychology as the children in the PATS study were at the beginning of their academic learning trajectory. If the dosage necessary to achieve decreased impulsivity is likely to have side effects that impair cognition for academic tasks and learning, the current "gold standard" treatment for ADHD, medication to control impulsivity and/or hyperactivity, may actually be contributing to the increased and persistent correlations between ADHD and difficulties with academic learning and performance (Miller et al., 2013; Molina et al., 2009; Willcutt et al., 2010).

This may prove to be a useful insight regarding the heterogeneity of behavioral manifestations of ADHD, including the behavioral versus cognitive windows of therapeutic efficacy, as well as some patients with ADHD not being responsive to reward-based interventions, lacking motivation to alter behaviors based on relationships or rewards, and lacking external goal motivations altogether. Given the different effects on cognition and motor behaviors, ongoing research with both adults and children is looking at the administration of methylphenidate, levodopa, or both in various conditions involving attention, motivation, and motor behaviors (Brown et al., 2010; Overtoom et al., 2003).

Other studies on medication efficacy for ADHD converge on inadequate response rates of 20% to 35% (Childress & Sallee, 2014). There are few studies of behavioral therapies with children and adolescents (Sonuga-Barke et al., 2013). In clinical, as compared with experimental, settings, the number of individuals who do not receive substantial benefit from medication for ADHD is not well studied. In one clinical study, approximately 21% of patients had discontinued medication, and the majority did so for psychological side effects, while the rest discontinued medication because the medication was not as effective as had been expected (Toomey, Sox, Rusinak, & Finkelstein, 2012). Those patients who do not receive benefit from one or more medication trials eventually do not return to have their prescriptions refilled, and they are generally lost to follow-up. It would be reasonable to assume, then, that the reported inadequate response rates are greater than shown in the experimental literature, which often excludes children with ADHD and comorbid conditions. Clinically, comorbid behavioral, mood, and learning disorders contribute to decreased quality of life and complicate treatment for children and adolescents with ADHD (Danckaerts et al., 2010).

These data lead to the conclusion that other treatment approaches are warranted and should be considered. Longitudinal studies indicate relatively poor practical clinical outcomes, with up to 65% of children initially diagnosed with ADHD still displaying some symptoms as adults, including both cognitive and functional impairment for everyday tasks (Clerkin et al., 2013). These findings provide ample reasoning to continue exploring additional evaluation and treatment methods for this patient population with a condition that does not necessarily resolve with age.

THE ROLE OF THE THALAMUS IN ADHD SYMPTOMATOLOGY

Among neuropsychologists, there is general acceptance that ADHD symptomatology is associated with altered functioning in the basal ganglia and associated cortical and subcortical networks that underlie attention and motor control of impulsive actions. Alteration of dopamine metabolism in these structures is a key contributor to the syndrome. Research on the role of the cerebellum in attention and motor responses continues to develop at a great pace (Koziol et al., 2014).

Some research was simply ahead of its time. In the 1960s, researchers demonstrated that cortical-thalamic-subcortical/basal ganglia feedback loops are involved in inhibitory control of behavior in both animals and humans (Sherman & Guillery, 2006). More recent work has demonstrated that even cortico-cortical connections are mediated by thalamic involvement (Sherman & Guillery, 2011).

The role of the thalamus in attention and impulsivity is beginning to come to light, and with it is the opportunity to bring together several previously separate streams of research (Sherman & Guillery, 2006). These include, but are not limited to, the modulatory role of the thalamus in both afferent and efferent signaling between the cortex and subcortical structures, such as the basal ganglia and cerebellum; the influence of the thalamus in the generation of the oscillatory complexes that result in the brainwaves measured by the electroencephalogram for both EEG and evoked response potentials (ERP) studies; and how these brainwaves are influenced by the availability and action of dopamine and other neurotransmitters.

Lesion studies have demonstrated unequivocally that waking-state EEG rhythms are generated at the level of the thalamus and that without the thalamic-cortical connections, nothing that is recognized as awareness, volition, or conscious thought is possible (Steriade & Deschenes, 1984). In addition to the behavioral symptoms common to most diagnostic checklists of ADHD behaviors, other common manifestations include poorly regulated sleep and states of daytime underarousal (Stephens et al., 2013). The thalamus is a key component of regulating states of arousal and alertness. Because children with ADHD often have comorbid sleep

problems and difficulty maintaining arousal and alertness in situations that are not intrinsically interesting to them, understanding the thalamic functions of children with ADHD is crucial. A common description of the mechanism for the effectiveness of stimulant medications is that they support a more normalized arousal state that allows for greater focus and impulse control. At the same time, a common side effect of medications is that the individual may have increased sleep difficulties, yet Stephens et al. (2013) documented that even unmedicated children with ADHD have sleep disturbances at a greater rate than do children without ADHD, thereby implicating the thalamus.

Ivanov et al. (2010) reported that patients with ADHD and controls had similar thalamic volume, although there were some regional differences, particularly in the bilateral pulvinar nuclei. Patients with ADHD who were medicated had somewhat larger thalamic volumes than those who had not been treated. The pulvinar-cortical and pulvinar-limbic connections contribute to arousal, selective attention, learning and memory, and orientation to visual and auditory stimuli. This area also contributes to decisions about the salience of visual objects and the filtering-out of nonsalient environmental distractors.

In a study of cortico-striato-thalamo-cortical loops using structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI), Xia et al. (2012) examined thalamic shape and white-matter connections of older children and adolescents aged 9 to 15 years old. The focus on the thalamus was due to its role in connecting the basal ganglia to the cerebral cortices and mediating the flow of information between and among various cortical networks. The authors described the specific thalamic role of controlling the flow of sensorimotor information during different waking and sleep states.

One leading hypothesis about hyperactivity is that children with ADHD are hypoaroused and that their hyperactivity is related to trying to keep themselves awake and alert. Rowe et al. (2005) found increased relative and absolute activity in the theta band range of EEG in adolescents diagnosed with ADHD, along with a relative decrease in beta band waves, thereby supporting the hypoarousal hypothesis. The authors suggested that this combination demonstrated both drowsy and alert states simultaneously and that this poorly modulated state contributes significantly to poor processing of information and the decreased ability to maintain attention. They connected their findings to dopamine metabolism, suggesting that dopamine suppresses locus coeruleus afferents to the thalamic reticular nucleus and that in persons with ADHD, the locus coeruleus has excess activity as well as enhanced activity of the thalamic reticular nucleus, causing reductions in cholinergic systems that ultimately result in hypoarousal.

Xia et al. (2012) found decreased mean fractional anisotropy and volume of the tracts between the thalamus and striatum, hippocampus, and prefrontal lobe in children with ADHD, and they confirmed Ivanov et al.'s (2010) findings of regional atrophy in the pulvinar complex. These differences were thought to contribute to disrupted attention and arousal problems found in persons with ADHD.

Studies of the thalamus in children with ADHD are rare in the literature. The adult literature has shown reduced activation of the thalamus during motor inhibition trials using BOLD measurement in adults whose ADHD persisted into adulthood after a diagnosis in childhood (Cubillo et al., 2010). DTI studies that demonstrated white-matter abnormalities in the caudate nucleus in children and adolescents with ADHD versus controls (Silk, Vance, Rinehart, Bradshaw, & Cunnington, 2009) showed no differences in whole thalamic volume. The authors hypothesized that the caudate differences, which began in middle to late adolescence, were delays, not absolute differences.

Mills et al. (2012) focused on cortical-striatal circuits mediated by the thalamus, particularly connections with the putamen. They investigated the role of spatial working memory in 67 children aged 7 to 11 years old who were diagnosed with ADHD or who were typically developing. Controlling for development and volume differences, they identified thalamic regions of interest (ROIs) for thalamo-cortical loops and used resting-state functional-connectivity functional MRI (fMRI) to define functional boundaries. Correlating thalamic connection strength with spatial span backward scores, the authors found that five areas of the thalamus in children diagnosed with ADHD showed connections that were significantly different from those of normal controls. While visual-spatial perception showed no difference in BOLD studies, the amount of activation and connectivity was significantly different in children with ADHD. These altered thalamic connections with the striatum and cortical regions were related to difficulties with working memory in many children with ADHD.

Mills et al. (2012) found that children with ADHD Combined type had stronger connections in thalamic ROIs and the putamen. The premotor-motor thalamic ROI, somatosensory thalamic ROI, and temporal thalamic ROI showed greater connectivity, and this hyperconnectivity was related to lower spatial span backward scores. In addition, aspects of the left putamen had atypical connections with multiple thalamic ROIs, and the authors surmised that these connections may be related to some of the behavioral impairments found in children with ADHD. They did not discuss whether this hyperconnectivity was perhaps compensatory or whether the hyperconnectivity itself may be part of the etiology of the behavioral problems.

Nevertheless, they emphasized the role of the thalamus as a mediating structure and emphasized that when functional connectivity is altered, this is likely related to altered communication between the thalamus and subcortical areas, as well as altered communication between the thalamus and the cortex, thereby resulting in dysfunctional regulation of behavior including, but not limited to, working memory.

Using a visual continuous performance test with 44 participants aged 9 to 15 years old with ADHD Combined type during fMRI, Li et al. (2012) found that reduced connectivity between the bilateral pulvinar and right prefrontal areas combined with increased connectivity between the right pulvinar and bilateral occipital areas are responsible for disrupted functioning in visual attention processing. Furthermore, the kind and degree of disruptions contribute to the observed inattentive symptoms of ADHD. Most curiously, even though these participants had ADHD Combined type, they did not make more commission errors than the typically developing controls. The significant difference was that the participants with ADHD Combined type made more omission errors.

Results of this study also showed that the bilateral pulvinar nuclei of the ADHD group showed decreased connectivity to the right prefrontal areas and significantly increased connectivity between the right pulvinar nuclei and bilateral occipital lobes. The Li et al. study (2012) did not evaluate working memory (see Mills et al., 2012) but visual sustained attention. Again, however, the areas involved in the particular focus of the task showed abnormally increased connectivity, suggesting that the enhanced connectivity may be a compensatory mechanism to make the attention that is being generated possible. Other findings were severe bilateral structural atrophy in the participants with ADHD, along with significant reductions in cerebellar activation. Although the high noise levels of the fMRI machinery as a contributing factor could not be ruled out, a strong reduction in blood flow to the auditory cortex during visual activity was found. Even so, the authors speculated that there may be significant differences in sensory suppressive mechanisms that contribute to the easy distractibility that characterizes ADHD.

Further developing the concept of an attentional network, De La Fuente, Xia, Branch, and Li (2013) reviewed the preceding and other literature in this area and concluded that the findings correlate well with clinical diagnoses. Their review highlights the central role of the pulvinar nuclei in both normal and abnormal functioning of attention and concentration.

Thus, the thalamus is not just a way station connecting the basal ganglia, the cerebellum, and the cortex. It plays a role in modulating excitatory and inhibitory functions of both the ascending and descending pathways to actively influence and modify behavioral outcomes. It is a crucial part of the networks that contribute to the common behavioral outcome identified as attention and concentration.

THE ROLE OF THE THALAMUS IN ADHD TREATMENT: GENERATOR OF THE EEG SIGNAL

An aspect of the thalamus that has been largely ignored in the attention literature is its role as the generator of the EEG signal (Steriade & Deschenes, 1984). The proliferation of deep brain stimulation (DBS) studies in awake humans is providing important information about the role of the thalamus in attention and reward processing (Lega, Kahana, Jaggi, Baltuch, & Zaghloul, 2011). Characteristics of pediatric EEG in ADHD are increasingly being documented, with findings that suggest differences between children with ADHD and normally developing controls. Furthermore, twin studies have shown that an excess of 4 Hz to 8 Hz frequencies has a high heritability (.77) and that this excess of 4 Hz to 8 Hz frequencies moderately correlates (.35) with behaviorally diagnosed ADHD (Tye, Rijsdijk, & McLoughlin, 2014). Buyck and Wiersema (2014) argue that findings such as this point to a deviant developmental trajectory, rather than a maturational delay. The very high heritability of ADHD in children (.88) and adults (.72) supports this position (Larsson, Chang, D'Onofrio, & Lichtenstein, 2014). These findings are particularly important for understanding the role of the thalamus in ADHD because the cortex itself does not generate these electrical waves. If the thalamus is removed, only slow delta waves remain (Villablanca & Salinas-Zeballos, 1972).

A precursor to the role of the EEG in self-regulation involved early research studies that measured EEG with deep brain implants and demonstrated that operant conditioning could reduce motor excitability and decrease impulsivity. Cognitive control of inhibition of impulsive behavior as well as sustained focus for a repetitive task has been demonstrated in animals using operant conditioning. Operant conditioning of reduction of motor hyperexcitability in humans has been demonstrated and replicated in small-*n* studies since the 1960s (Sterman, 1981, 2010; Sterman & Clemente, 1961; Sterman at al., 1970). Recent advances in functional imaging are allowing researchers to demonstrate how these operant-conditioning techniques result in long-lasting modification of deregulated neural oscillations that lead to hyperexcitability and inattentive and impulsive behaviors.

Research from the 1970s demonstrated that operant conditioning that increased sleep spindles also led to increased control of impulsivity for executing goal-driven motor functions and a quiet alert mental state (Howe & Sterman, 1972, 1973; Lucas & Sterman, 1974). In a

serendipitous experimental observation, cats trained to produce increased sleep spindles were found to be more resistant to seizures when exposed to an epileptogenic substance compared with cats that had not undergone the specific operant-conditioning training. A connection between increased nighttime sleep spindles in Stage 2 sleep was shown to be correlated with waking-state changes in motor excitability, and data revealed that operant-conditioning training was the cause (Howe & Sterman, 1972, 1973; Sterman et al., 1970).

This finding has relevance to ADHD evaluation and treatment in that it was repeatedly shown in experiments with animals that had no possibility of secondary gain that it was possible for an animal to learn self-regulation of motor excitability and motor impulsiveness through operant-conditioning techniques. Most of the early work in this area was focused on raising the threshold for seizures for workers exposed to a toxic substance in rocket fuel. Several studies were done with patients with intractable seizures, including an A-B-A design where seizures were trained to decrease in several patients, then increased again in those same patients using the same operant-conditioning techniques to lower the threshold for motor seizures, and then were retrained to raise the threshold, thereby resulting again in fewer seizures (Sterman, 2010). Although that study can no longer ethically be replicated, peer-reviewed studies have shown that operant conditioning can be effective in reducing seizure frequency to a level at which patients are able to obtain driver's licenses, a real-world outcome with clinical significance (see Sterman, 2010, for review). Interest in this technique is reviving as the cognitive side effects of long-term administration of antiepileptic medications become increasingly unacceptable, especially when administered to children.

The EEG is seeing expanded use in neuroscientific studies because its millisecond temporal resolution is not achievable in fMRI and other functional imaging. EEG studies, including ERP, are also being used simultaneously with functional imaging to understand the temporal and directional aspects of the static pictures that other methods produce (Karch et al., 2014; Levesque, Beauregard, & Mensour, 2006). The EEG is comparatively child-friendly because it is noninvasive, can be done without large, loud machinery, and is relatively more forgiving of some body movement.

With the advent of DBS studies, mostly in adults, in-vivo recordings can also be done to understand the direct functioning of the signals in human tissue, rather than having to rely solely on animal models. An example of this advance in understanding attention and reward processing was described by Lega et al. (2011), in which visual reward images of an awake adult patient with treatment-resistant depression, another condition in which reward processing is considered to be aberrant, was evaluated. The authors used in-vivo DBS while the participant played a video game. The ventral striatum was evaluated as a site for processing reward information. Lega et al. found that in this one depressed adult, local field potentials indicated that oscillations in the alpha range were sensitive to positive feedback, whereas beta and theta oscillations were increased during unrewarded trials. Lega et al. also observed an alpha-gamma cross-frequency coupling that differentiated positive from negative feedback. It should be noted that there is aberrant processing of rewards in depression as well as in ADHD and no one has yet researched the different deviant responses to rewards in ADHD using DBS in an awake child.

These findings showed an electrophysiological basis for different EEG patterns during positive, negative, and neutral reward conditions and showed that these patterns can be differentiated not only by location and magnitude, but also by specific patterns of relationships that occur during the different reward conditions. In both animal studies (Sterman, 1981; Sterman et al., 1969) and human studies (Lantz & Sterman, 1988; Sterman, 2010), it has been shown that it is possible to learn to self-regulate specific frequency bands. This in turn, leads to the possibility that aberrant patterns of processing may be amenable to resetting through operant conditioning in a carefully constructed and monitored set of behavioral exercises with appropriate feedback for performance given within an optimal time window after achieving a specific target state.

A review of the literature of self-regulation of EEG frequencies by children and adults diagnosed with ADHD is beyond the scope of this article. In a recent review article, Loo and Makeig (2012) examined the EEG and the theta-beta band ratio as a diagnostic tool in ADHD and concluded that it is not yet ready as a stand-alone evaluation, although there are promising developments with this tool. There is increasing evidence that learning self-regulation of EEG frequencies in ADHD populations results in a specific effect, especially for inattention and impulsivity, but not for hyperactivity (Arns, Heinrich, & Strehl, 2014).

SUMMARY

ADHD is a chronic disorder that has persistent symptoms of inattention and impulsivity that do not remit with age, although hyperactivity, if present, does tend to remit over time. Furthermore, longitudinal studies have demonstrated that various treatment modalities (medication, cognitive-behavioral therapy, and medication with behavioral training) showed no differences in functional outcome over time. Medication therapy has been shown to improve behavioral control

at increased doses but at a cost of interference in cognitive functioning. Finally, studies have shown that the majority of children diagnosed with ADHD will display continued cognitive and functional impairments associated with ADHD into adulthood.

In reviewing pertinent research in ADHD, it is clear that the thalamus plays a prominent role in ADHD symptomatology. Most brain circuitry is mediated by the thalamus, including feedforward and feedback loops between various neural circuits that connect areas of the cortex and basal ganglia as well as cortico-cerebellar loops. Cortico-cortical connections are also mediated by the thalamus. Importantly, the thalamus generates waking-state EEG rhythms, strongly indicating that thalamic influence on neural circuitry connections is active and prominent. Given these findings, the thalamus likely has a prominent role in ADHD symptomatology. ADHD studies have consistently shown abnormalities in the thalamic pulvinar nucleus.

The thalamus plays a central role in the modulation of behavioral response to environmental stimulation and is also the source of the EEG signals that are measured from scalp electrodes. DBS studies have shown differential effects of rewards and nonrewards trials on the EEG, and research dating back to the 1960s on animals and humans has demonstrated that it is possible to learn self-regulation of aspects of EEG oscillations in a way that modifies both states and behaviors. Controversy exists for alternative interventions such as neurofeedback as a behavioral intervention for enhancing the ability to self-regulate attention and impulsivity. However, careful review of the efficacy of current ADHD treatments and the evidence that both humans and animals have the ability to self-regulate EEG oscillations suggests that there is a reasonable research basis for further investigation and implementation of learned self-regulation of motor impulsivity and attentional focus.

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