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Changing Behavior, Brain Differences, or Both?

A Review of Effective ADHD Treatment

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Honors Senior Thesis

Abstract

Much debate exists over the proper course of treatment for individuals with attention-deficit/hyperactivity disorder (ADHD). Stimulant medications, such as methylphenidate (e.g., Ritalin) and amphetamine (e.g., Adderall), have been shown to be effective in managing ADHD symptoms. More recently, non-stimulant medications, such as atomoxetine (e.g., Strattera), clonidine (e.g., Kapvay), and guanfacine (e.g., Intuniv), have provided a pharmacological alternative with potentially lesser side effects than stimulants. Behavioral therapies, like behavioral parent training, behavioral classroom management, and behavioral peer interventions, have shown long-term benefits for children with ADHD; however, the success of the short-term management of ADHD symptoms is not as substantial when compared with stimulant medications. Continued research suggests that combined treatment with active and intensive behavioral therapy and lower doses of stimulant medication may yield the highest ADHD treatment success rates. More evidence needs to be gathered to determine whether this is the optimal treatment plan.

Changing Behavior, Brain Differences, or Both?

Attention-deficit/hyperactivity disorder (ADHD) is a disorder that is estimated to affect roughly 5% of children in most cultures and manifests fairly early on in childhood (American Psychiatric Association, 2013). Recent studies have supported a model of the disorder with a unitary ADHD component and two separable and specific dimensions of inattention and hyperactivity-impulsivity (Burns et al., 2014; Toplak et al., 2012). This model supports the current view of ADHD as one single disorder with two relatively distinguishable sets of symptoms. The diagnostic criteria for ADHD require that symptoms from one, or both, of the dimensions be present before the age of twelve years (American Psychiatric Association, 2013). This can lead to one of three possible diagnoses: predominantly inattentive, predominantly hyperactive/impulsive, or combined presentation.

In addition to the inappropriate levels of inattention, hyperactivity, and impulsivity that characterize individuals with ADHD, research also suggests children with ADHD face developmental and neuropsychological difficulties (Weyandt & Gudmundsdottir, 2014). The direct cause of ADHD is not yet known; however, researchers are beginning to agree on a multitude of factors that can contribute to a higher risk of the disorder and a greater expression of the symptoms.

Etiology of ADHD

While it is generally agreed upon that ADHD can be caused by many different factors, research strongly suggests that it is a neurodevelopmental disorder primarily influenced by genetic and neurobiological factors (Faraone, 2014; Kieling, Gonclaves, Tannock, & Castellanos, 2008; Scasselatti et al., 2012). In fact, a hypothesis that has seen much support as a

cause of ADHD is that children with ADHD show differences in brain structure and function compared to children without ADHD. The three brain areas that are primarily implicated in ADHD as showing deficits are the prefrontal cortex, the caudate nucleus, and the cerebellum (Sharma & Couture, 2014; Hendren, De Backer, & Pandina, 2000).

Based on past twin studies, the evidence for there being a genetic basis for ADHD is becoming stronger (Swanson et al., 2000). More research needs to be done, but the genetic studies show that diagnosis of ADHD is associated with polymorphisms in some dopamine genes (Swanson, Castellanos, Murias, LaHoste, & Kennedy, 1998). These variations in dopamine genes have been shown to have an effect on volume of the prefrontal brain regions, which are often reduced in children with ADHD (Durston et al., 2005). Due largely to these genetic studies, ADHD is thought to have its basis in the dopaminergic system of the brain. Individuals with ADHD report that they cannot pay attention to topics that they find uninteresting, and researchers believe that a cause of this inattentiveness and distractibility symptom is an insufficient amount of dopamine in the prefrontal cortex (Hunt, 2006). Normal individuals with proper dopamine levels in the mesocortical areas have the abilities to attach attention and actively suppress distractions, abilities that are absent in individuals with ADHD (Hunt, 2006).

Despite the strong support for brain differences as a possible cause of ADHD, the variation in brain structure and function between brains is often significant and the rate of brain development will vary even in healthy brains. However, it is generally agreed upon that ADHD does have its basis in biological causes. This consensus supports management of ADHD symptoms through the alteration of these abnormal brain discrepancies, very often through the employment of medication as treatment.

Medication Treatments

The use of medications to treat symptoms of ADHD in children has been debated heavily. Many in opposition to the use of medications argue that they are overprescribed, lead to overdiagnosis of ADHD, and lead to later substance use, among other contentions (Parens & Johnston, 2008). While concerns are valid and understandable due to the anxiety associated with a diagnosis in oneself or a loved one, the Council of Scientific Affairs of the American Medical Association found that there was little evidence of overprescription by physicians or of overdiagnosis or misdiagnosis of the disorder itself (Spencer, Biederman, & Wilens, 2000). Due to this lack of strong evidence opposing the use of medication as treatment of ADHD symptoms, they are often used widely and successfully in the treatment of this disorder. Historically and still predominantly, stimulant medications are the choice treatment. However, recent research has brought forth non-stimulants that are showing positive effects in the treatment of ADHD symptoms.

Ritalin -- methylphenidate

Methylphenidate (Ritalin) has been proven effective for treatment of ADHD symptoms (Parker, 2013), and it is the most commonly prescribed stimulant medication (Greydanus & Merrick, 2009). This medication is used as a treatment of ADHD symptoms because it has been measured to increase the release of dopamine in target areas, such as the striatum and prefrontal cortex (Viggiano et al., 2004; Tripp & Wickens, 2009). Methylphenidate accomplishes this in the central nervous system as an indirect agonist by acting as a dopamine reuptake inhibitor to block the dopamine transporter. By blocking the reuptake of the monoamines dopamine and noradrenaline, methylphenidate increases the amount of these monoamines in the synapses in the

prefrontal cortex and dorsal striatal areas of the brain. The increased activation in these areas is widely thought to be the reason that methylphenidate works so well to ameliorate the symptoms of ADHD, like hyperactivity and inattentiveness.

Methylphenidate is approved for the treatment of ADHD symptoms in children age six or older in the United States (Moore, 2010). Compared to other medications—primarily non-stimulants—methylphenidate appears to have a greater impact on ADHD symptoms, and the medication is generally well tolerated by children with ADHD (Bedard et al., 2015; Yildiz, Sismanlar, Memik, Karakaya, & Agaoglu, 2011).

Adderall – amphetamine

Another common stimulant medication for the treatment of ADHD symptoms is a combination of the two enantiomers of amphetamine (Adderall). Methylphenidate and amphetamine are both seen as effective in the treatment of ADHD symptoms; however, they do this through slightly different mechanisms (Sharma & Couture, 2014). Both stimulant medications inhibit monoamine oxidase, but amphetamine is the more potent of the two (Pliszka, 2005; Pelham et al., 1999). Research has also found that once-daily amphetamine was similar to twice-daily methylphenidate in its management of ADHD behavioral symptoms (Bauchner, 2000).

Low doses of amphetamine are typically used initially, and the doses are gradually increased until the minimum dose required to produce optimal effects is found (Moore, 2010). Due to its higher potency, both the maximum recommended daily dose of amphetamine and the optimal daily dose of amphetamine are less than the suggested or required daily doses of methylphenidate (Findling, Short, & Manos, 2002).

Non-stimulant Medication Treatments

Some individuals faced with ADHD symptoms may not respond to stimulant medications, they may find stimulants intolerable, or they may have an aversion toward stimulants because they are a controlled substance. In fact, research shows that 10-30% of all children and adults with ADHD either do not respond to or do not tolerate treatment with stimulants (Banaschewski, Roessner, Dittmann, Santosh, & Rothenberger, 2004).

For this subset of individuals with ADHD, non-stimulant medication may be an alternative. FDA approved non-stimulants for the treatment of ADHD are atomoxetine (Strattera), extended-release α-2 agonist clonidine (Kapvay) and guanafacine (Intuniv). These non-stimulant medications do not have the abuse potential of stimulants, and non-stimulants are generally better tolerated than stimulants (Sharma & Couture, 2014). Most current research favors stimulant medication, but this is less due to non-stimulant inferiority—which has dubious support due to different study methodologies and outcome measures—and more because non-stimulants normally take several weeks to show their full effects (Sharma & Couture, 2014). Atomoxetine is the best evaluated non-stimulant medication for the treatment of ADHD symptoms (Banaschewski et al., 2004). In a recent meta-analysis, the effectiveness of atomoxetine for children and youth with ADHD was shown to be effective in fifteen clinical trials from four different global regions (Tanaka, Rohde, Jin, Feldman, & Upadhyaya, 2013). The efficacy of these non-stimulant medications in comparison to stimulant medications needs to be examined further; however, it is becoming increasingly understood that non-stimulants provide an alternative treatment for ADHD symptoms.

Optimal Treatment of ADHD with Medication

Medications are not the answer or cure for the disorder. Several questions still remain about their long-term benefits (Jensen et al., 2007). However, their short-term benefits have been supported extensively in the literature (Spencer, Biederman, & Wilens, 2000). In fact, 65-75% of children with ADHD respond to any single medication, and this success rate can rise to 80-90% with the trying of a second medication for those who did not initially respond (Connor, 2014).

In McCluskey and McCluskey's book, one parent of a child with ADHD summed up the use of medications well when they said: "Ideally, stimulants should be prescribed, monitored carefully, and there should be ongoing communication with parents and school personnel" (cited in Mash & Wolfe, 2013). Medications, both stimulant and non-stimulant, are a powerful weapon against the symptoms of ADHD. However, like any medication, proper compliance and usage are important factors for this topic of treatment of ADHD symptoms. Further research needs to be done examining proper dosage, long-term efficacy, side effects, and the use of medication in both younger children and adults with ADHD.

Nevertheless, medications are among the most effective treatments for ADHD symptoms. Medications do not, however, address many of the social, familial, or contextual problems that present themselves to children with ADHD. It is in the management of these problems that behavioral therapy is useful as a primary intervention.

Behavioral Therapy

While medication treatment ameliorates the symptoms of ADHD in the short-term, there is no clear evidence that medications lead to improved long-term academic achievement (Pelham, 1999). However, evidence-based behavioral interventions could provide long-term

symptom relief. A recent literature review concluded that behavioral parent training, behavioral classroom management, and intensive peer-focused behavioral interventions were all well-established treatments for children with ADHD (Pelham & Fabiano, 2008).

Behavioral Parent Training

Many of the theories behind the causes of ADHD are focused on biological and genetic factors; however, researchers are beginning to understand how genetic susceptibility and environmental influences impact the development of ADHD and the exacerbation of ADHD symptoms (Nigg & Barkley, 2014). When considering children with ADHD, much of the environmental influence is due to familial or home factors, because a child is in the home environment frequently early on in development. It then makes sense that research suggests family factors and parental styles play an important role in understanding ADHD (Johnston & Chronis-Tuscano, 2014; Mash & Johnston, 2005).

Chacko et al. (2014) discuss several reasons why behavioral parent training (BPT) works for parents of children with ADHD. These reasons are focused on a cycle of parent-child behaviors. Disruptive behaviors consistent with ADHD symptoms can often cause stress and conflict between parents and families, while negative parental attitudes toward the child can lead to maladaptive parenting styles that further intensify the severity of ADHD symptom behaviors. It is because of this maladaptive cycle that BPT is warranted and effective for families of children with ADHD.

There are many different procedures and BPT programs; however, they mostly share a similar theoretical foundation based on operant and social learning theories (Garland, Hawley, Brookman-Frazee, & Hurlburt, 2008). The goal of most BPT programs is to provide parents with

a variety of skills to help them in the challenge of parenting a child with ADHD. This usually begins with psychoeducation. Information about ADHD, how the disorder affects the child and others around the child, and common treatments for the disorder all help the parents to develop effective parenting practices. Parents are also taught how to manage their child's oppositional and noncompliant behaviors. Positive reinforcement techniques, such as specific praise and token reward systems, are introduced to increase the frequency of desired behaviors from the child. Conversely, inattention in response to attention-seeking behaviors and effective positive punishment, like time-out, are taught to parents to decrease the frequency of undesired behavior (Chacko et al., 2014; Garland et al., 2008).

Behavioral Classroom Management

Other than the home and familial environment, children spend most of their time in a school environment. Whereas ADHD symptom behaviors can be disruptive at home, they can also be disruptive with teachers and classmates at school. The focus of behavioral classroom management (BCM) is to manage behaviors that interfere with learning and to provide an environment that capitalizes on the student's strengths (DuPaul, Stoner, & Reid, 2014).

Many of the techniques used in BPT are also effective interventions in BCM. Positive reinforcement interventions, like token reward systems, and positive punishments, like time-out, can be used by teachers in ways similar to how a parent would use them (Chacko et al., 2014; Pfiffner & DuPaul, 2014; DuPaul, Stoner, & Reid, 2014). One common way for teachers to acknowledge student behaviors and consequently reward or punish them through a token system is through the use of Daily Behavior Report Cards (DBRCs) which are shown to significantly increase on-task behavior in children with ADHD (DuPaul, Stoner, Reid, 2014; Pfiffner &

DuPaul, 2014; Jurbergs, Palcic, & Kelley, 2010). A BCM intervention approach is also concerned with the students' academic performance. Some evidence-based interventions that teachers can implement to increase the academic performance of children with ADHD are changing the classroom environment, actively teaching expectations, adjusting assignments, and adjusting instructional strategies (Pfiffner & DuPaul, 2014; DuPaul, Stoner, Reid, 2014).

Behavioral Peer Interventions

Behavioral therapies such as BPT and BCM address ADHD symptoms from the perspectives of parents and teachers; however, peers can also have strong and essential interactions with children with ADHD. Disruptive behaviors and ADHD symptoms can have a negative effect on interpersonal relationships with peers simply due to the nature of the "annoying" behaviors. Individual or group-based social skills training have proven ineffective in producing beneficial effects for children with ADHD (Pelham & Fabiano, 2008).

However, intensive summer treatment programs have been shown to have a positive effect in targeting peer relationships and functioning in a recreational setting (Pelham & Fabiano, 2008). These summer treatment programs are usually camp-like settings that maximize opportunities to build peer relationships. This type of intervention has been shown to be effective in producing meaningful changes in child behavior, social skills, and peer relationships (Pelham et al., 2010).

Effectiveness of Behavioral Therapy in the Treatment of ADHD

Unlike medication treatment where the concurrent use of several different medications is not likely to have an additive effect on ADHD symptoms, simultaneous implementation of different forms of behavioral therapy does seem to be effective. Jurbergs, Palcic, and Kelley

(2010) found that the greatest increase in on-task behavior following the use of DBRCs occurred in the treatment group where parents were involved in the review of the DBRC and the implementation of rewards for desired behavior. This additive effect of behavioral interventions is most often seen through the use of BPT and BCM, where home-school communication and cooperation concurrently reinforce desired behaviors and academic goals (DuPaul, Stoner, Reid, 2014). The use of BPT, BCM, and BPI in conjunction with each other is an effective, evidence-based intervention for the treatment of ADHD symptoms, because it addresses the wide array of environmental factors that influence, and are influenced by, children with ADHD.

Conclusion: Effective Treatment of ADHD using both Behavioral Therapy and Medication

One study revealed that a stimulant medication treatment group and a combined group receiving both behavior therapy and stimulant medication showed significant improvement in ADHD symptoms, and both groups were superior to the behavior therapy only and control groups (MTA Study Group, 1999). However, other research has shown no significant differences in ADHD symptoms between a treatment group receiving behavioral therapy and a group receiving both behavioral therapy and stimulant medication. In this study, almost all children were rated as having diminished symptoms, and the treatment was seen as beneficial by parents of all children (Pelham et al., 2000). Pelham et al. (2000) suggested that medication did not show large effects beyond behavioral intervention when the behavioral intervention was active and intensive.

Furthermore, concurrent behavioral intervention diminished the incremental effects of stimulant medications beyond low to moderate doses (Pelham et al., 1999; Dopfner et al., 2004). Pelham et al. (1999) showed an increased effect of stimulant medication beyond behavioral

intervention; however, it suggests that lower doses of the medication are needed when used in conjunction with effective behavioral therapy. In one study that examined individually tailored adaptive and multimodal intervention for children with ADHD, researchers found evidence that high success rates could be found after combined treatment, even if separate behavioral therapy or medication treatment had been less effective (Dopfner et al., 2004). Yet another researcher concluded that medications should be used as part of a larger intervention plan for children with ADHD, along with things like behavioral parent training and school consultation (Connor, 2014).

Medications may be preferred in the short-term management of ADHD symptoms, but proper and intensive behavioral therapy receives much support in the literature as a long-term treatment for improving the symptoms of ADHD. Recent literature shows the merits of combined behavioral therapy and medication intervention (Smith & Shapiro, 2014). It may very well be the case that treatment plans need to be carefully individualized and optimized for each individual with ADHD. Clearly, much more research needs to be done to determine the optimal treatment plan for children with ADHD.

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