



Interventions in ADHD: A comparative review of stimulant medications and behavioral therapies



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ABSTRACT

ADHD has a prevalence of approximately 10% in children with evidence supporting its continuance into adulthood. This has a significant impact on how we address treatment at substance abuse facilities and also has implications for personal and occupational functioning. A lack of evidence to support the superiority of any one intervention over the other has created difficulties for both clinicians and parents. A recent review highlights long-term and short-term outcomes (Craig et al., 2015). This article reviews the benefits and pitfalls of both pharmacological interventions and behavioral therapies in the treatment of ADHD. Key articles were reviewed on the benefits and side effects of stimulants, the methods and benefits of behavioral interventions, and the effects of combination therapy. Google Scholar, PsychINFO, Medline, Cochrane, and CINAHL were searched with the following search words: Attention Deficit Hyperactivity Disorder, ADHD, Stimulant Medication, Behavioral Interventions, Combination Therapy, Cognitive Therapy, Functioning and Growth. It was found that stimulants are very effective during the period in which they are taken. While short term benefits are clear, longer term ones are not. Behavioral interventions play a key role for long-term improvement of executive functioning and organizational skills. There is a paucity of long-term randomized placebo controlled studies and current literature is inconclusive on what is the preferred intervention.

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1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) affects the lives of millions of children and adults throughout the world. Current evidence suggests a prevalence of 10% in all children (Faraone et al., 2003). It is found in 3% to 5% of school aged children and accounts for 30–50% of referrals to child psychiatry services (Mash and Barkley, 1996; Talbott et al., 1988). In a comprehensive review, Faraone and Biederman reported a prevalence of 3.2% for a full diagnosis and 6.6% for a partial diagnosis of adult ADHD (2005). The National Comorbidity survey found the prevalence of adult

ADHD to be 4.4% (Kessler et al., 2006). This is believed to be our best current estimate (Faraone and Biederman, 2005).

It is important to note that there is high prevalence of adult ADHD despite the disease being one the most diagnosed and treated disorders in children (Mash and Barkley, 1996; Talbott et al., 1988). While the ultimate goal of treatment of any disorder is cure, in mental health the outcome measures are different. This raises questions about the efficacy of the current interventions in childhood ADHD.

In analyzing the efficacy interventions, we looked at the two available modalities of treatment; stimulant medication and behavioral therapy. The components of pharmacological intervention were compared with combination therapy. This review will help bridge the gap in knowledge for physicians and parents while weighing the evidence to make an informed judgment on treatment options.

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2. Objectives

1. To review literature for evidence on the use of stimulants and behavior interventions.
2. To review literature on the long term and short term side effects of stimulant medications.
3. To review literature on studies that has compared stimulants to behavioral interventions and their combination effect.
4. Summarize the evidence.

3. Methodology

We reviewed existing literature and key articles on treatment strategies for ADHD and the side effects of stimulant treatment; short term and long term. We searched Google Scholar, PsychINFO, Medline, Cochrane, and CINAHL. We used for our search combinations of the following keywords: “stimulants,” “Methylphenidate,” “multimodal treatment,” “ADHD,” “behavioral interventions,” “combined therapy,” “CBT,” “OST,” “long term effects,” “side effects,” and “benefits”. A study was considered eligible for inclusion if the disorder being addressed fulfilled DSM-IV criteria for ADHD; treatment was with stimulants; behavioral methods; or both; and the results were concluded in a systematic and reproducible manner. Overall; 80 studies were reviewed; of these; we used 20 studies on the different effects of stimulants in the treatment of ADHD. 10 studies on the effects of behavioral interventions and 5 studies on the effects of combination therapy were used.

4. Results

4.1. Stimulant medications

4.1.1. The benefits

Stimulants have been used in the treatment of childhood ADHD for about 70 years (Bradley, 1937). They are mainly composed of Methylphenidate and Amphetamine compounds. These medications in the treatment of ADHD have been extensively studied and have proven to have significant short term efficacy for all degrees and subtypes of ADHD (Garland, 1998; Spencer et al., 1996). In a randomized double-blind placebo-controlled study of the role of stimulants in the treatment of ADHD it was found that there were ongoing positive effects 15 months after onset of treatment (Gillberg et al., 1997). There is also evidence supporting sustained benefits 3 years post treatment. After 3 years, there was no clear evidence of the effects of the 14 month randomization (Craig et al., 2015; Murray et al., 2008). However, the scope of these studies may have been limited due to issues with recruitment and retention. In conducting research, comparing treatment interventions that include CBT and other psychotherapies the primary difficulty is in controlling the populations. It is important to mention that these studies did not highlight patient characteristics.

4.1.2. Executive functioning/organizational skills

There are cross-sectional studies showing benefits with the use of stimulants in executive functioning in children with ADHD-Combined type. However, the data for the long term benefits regarding organizational skills and executive functioning is scarce and lacks clarity (Craig et al., 2015; Vance et al., 2003).

4.1.3. Substance abuse

A decrease in the risk of substance abuse was reported for patients stimulants (Craig et al., 2015; Wilens et al., 2003). However, more recent studies showed that medication did not

affect the risk for substance use in adolescence (Molina et al., 2013). The studies do not concur on efficacy of interventions.

4.1.4. Academic performance

Stimulants appear to improve short-term academic performance although the impact on ultimate academic achievement is less clear (Craig et al., 2015). Some studies could not find an association between the two (Loe and Feldman, 2007), but another study (Zoëga et al., 2012) have described improvement in:

1. Test taking ability.
2. Concentration.
3. Listening.
4. Note-taking.

One study states that stimulants improve behavior in the classroom but not at home (Efron et al., 1997). This is described as the ability to “show what they know” rather than an increase in learning potential (Craig et al., 2015). Another study provides evidence of improvement that is maintained for 2 years with continuous stimulant treatment (Schachar et al., 1997).

4.1.5. Imaging studies/neurobiological changes

Neurobiological changes in imaging studies point towards a protective role for stimulant treatment against cortical thinning (Craig et al., 2015). It has been suggested that stimulants are associated with:

1. The normalization of posterior inferior cerebellar vermis (Bledsoe et al., 2009).
2. Right ACC () normalization (Schnoebelen et al., 2010).
3. Normalization of splenium size (Schnoebelen et al., 2010).
4. Reduction of basal ganglia surface deformations (Sobel et al., 2010).
5. Decrease in white matter of un-medicated patients (Castellanos et al., 2002).

Overall, stimulants when prescribed in their therapeutic doses decrease changes in brain structure in subjects with ADHD (Frodl and Skokauskas, 2012; Spencer et al., 2013). These medication-associated brain effects may be the reason for the clinical benefits of stimulants. However there is still lack of clarity (Frodl and Skokauskas, 2012).

4.1.6. Quality of life

The assessment of quality of life and improvements elated to it are always difficult to assess. While stimulants have a positive effect on the quality of life of children during treatment, they never achieved parameters of the normal controls (Klassen et al., 2004; Shaw et al., 2012). In conclusion, there is no evidence to support lasting improvements (Craig et al., 2015).

4.1.7. Functioning and growth

The evidence around improvement of functioning lacks consistency (Craig et al., 2015). Our best source on the matter comes from the MTA study, which suggests early functioning improvement that is maintained at the 8 year follow-up, but overall lower functioning when compared with normal controls (Molina et al., 2009). There is no evidence that stimulants are associated with differences in growth rates (Harstad et al., 2014).

4.1.8. Long term benefits

Short-term benefits of stimulants are well described in contrast to long term benefits. There are many limitations in conducting proper studies, that results in a paucity of evidence of long-term outcomes (Parker et al., 2013). Studies show no academic or

emotional status improvement after 2 years with stimulants (Hechtman et al., 2004). Stimulants demonstrate long term efficacy after 2 years of treatment but no significant improvement in ADHD symptoms (Abikoff et al., 2004). However, it is important to note that the absence of data does not mean absence of efficacy. There is a lack of evidence for ADHD symptom improvement after 2 years, and the majority of studies that we have now describe no changes in symptom severity (Abikoff et al., 2004; Molina et al., 2009; Parker et al., 2013). Overall, it is clear that lack of treatment causes poorer long term outcomes. Studies show that treatment may improve the long term outcome for some individuals and certain subtypes but not to the level of healthy controls (Shaw et al., 2012).

4.1.9. The adverse-effects and drawbacks

The main concern when stimulants are prescribed are their side-effects as well as their effects on comorbid conditions (Craig et al., 2015). Main adverse effects of stimulants are (Efron et al., 1997):

1. Appetite suppression, being the most severe.
2. Insomnia.
3. Irritability.
4. Proneness to crying.
5. Anxiousness (sadness/unhappiness).
6. Nightmares.

These are usually well tolerated throughout treatment (Efron et al., 1997). Delinquency was found to be higher in children who took medication at the 36 month follow up in the MTA study, though the association is not completely clear (Molina et al., 2009). Studies have associated stimulants with negative mood changes becoming apparent around 4 months after the start of treatment (Schachar et al., 1997). Stimulants also do not decrease the risk of substance abuse in adolescence or adulthood amongst the high risk ADHD patient population (Molina et al., 2013).

Long term side effects are not well researched (Craig et al., 2015). The lack of data is alarming especially when long term benefits of stimulants are not established clearly. There is a need for well-designed studies to answer these questions (Craig et al., 2015).

4.2. Behavioral interventions

The efficacy of behavioral therapy in the treatment of ADHD is a matter of controversy. There are a wide range of therapies which fall under the term “behavioral interventions” (this includes Cognitive Behavioral Therapy, Meta Cognitive Therapy, Psychosocial Therapy, Organizational Skill Training, Multimodal Psychosocial Treatment). This review, however, does not individually explore the efficacy of the different interventions, rather, the different behavior interventions were reviewed under the heading of “Behavioral Interventions”. The authors focused on their collective efficacy and role. There were very few studies looking into the effect of CBT (Cognitive Behavior Therapy) in un-medicated ADHD patients (Solanto et al., 2010).

4.2.1. Organizational skills, academic proficiency and functioning

In childhood (Solanto et al., 2010), a study reviewing meta-cognitive therapies showed significant benefit in patients whether medicated or not. This paper focused on inattention symptoms that are better defined as organization, time management, and planning (OTMP). Another study concluded that behavioral treatment targeting a similar symptom subgroup i.e.; OTMP, in un-medicated children with ADHD improved long term

functioning (Abikoff et al., 2013). The authors propose that it may soon be used clinically in children with ADHD.

In adolescence, there were similarities in the reported effects between organizational skill training as evidenced in improved homework related performance and academic achievement (Abikoff et al., 2013; Hechtman et al., 2004). OST also improved family communication and reduced conflict (MTA Cooperative Group, 1999). The social improvement was reported by family members who noticed positive change in conduct (MTA Cooperative Group, 1999; Weiss et al., 2012). Gains in organizational skills and academic performance were sustained during the 7–12 month follow up period (Abikoff et al., 2013).

In adulthood, a randomized controlled trial of CBT therapy concluded that CBT improved outcomes in un-medicated patients regarding both core symptoms (such as hyperactivity, impulsivity, inattention, and ODD) and functioning (Weiss et al., 2012). This suggests that CBT is an effective treatment for adults with ADHD (Weiss et al., 2012). Keep in mind that functional improvement was measured on the Sheehan Disability Scale, a well validated scale measuring social, family, and work functioning (Weiss et al., 2012). It seems that behavioral methods of treatment have the potential of long term benefits if applied properly and sustained until adopted by patients in their day-to-day lives (Abikoff et al., 2013).

4.2.2. Adverse effects and drawbacks

There are no reported somatic adverse effects for behavioral therapy. However, it is possible that even non-pharmacological interventions can have side effects that may manifest in ways hitherto unrecognized.

The studies that used behavioral interventions didn't report adverse effects regarding psychological impacts or patient relapse (Abikoff et al., 2013; Solanto et al., 2010). Psychotherapy does have cost implications and subjectivity. It still lacks controlled studies, standardized methods, and has many confounding variables. Behavioral and psychosocial interventions in children with moderate to severe ADHD resulted in mild improvements in hyperactivity and impulsivity symptoms but improvements were less apparent for inattention symptoms. These benefits were not as prominent as those seen with pharmacological and combined interventions. It is important to note that the benefits were marked in mild ADHD (Swanson et al., 2001). It is also important to note the various challenges and difficulties that face studies that target children with mild to severe ADHD. Adherence to treatment, cooperation of school staff and parents, and maintaining control in the school setting were some of the many challenges that met researchers (Arnold et al., 1997; Swanson et al., 2001).

4.3. Combination therapy

In a study by Klein and Abikoff involving 89 children with ADHD, it was concluded that methylphenidate and stimulant/behavioral therapy combination treatments were significantly superior to behavior therapy (1997). It also found that in certain situations, the combination was superior (Klein and Abikoff, 1997). The MTA 14 month randomized trial stated that combined treatment did not offer significantly greater benefits than medication management for core ADHD symptoms, but improved functioning and family-related outcomes especially in children with anxiety related disorders (MTA Cooperative Group, 1999; Weiss et al., 2012). It also highlighted significantly lower doses of stimulants used in combined treatment (MTA Cooperative Group, 1999). In contrast to these studies, one trial was not able to demonstrate that medication improves the outcome of CBT for adults with ADHD (Weiss et al., 2012). There was no evidence supporting the addition of psychosocial intervention to improve ADHD symptoms in children who responded to stimulant

treatment (Abikoff et al., 2004; Schachar et al., 1997). It was found that psychotherapy when added to stimulants did not improve academic or emotional outcomes (Schachar et al., 1997).

It is possible that the lack of uniformity in the modalities of interventions could contribute to the lack of consistency in outcomes. Also, the development of CBT as an intervention in recent years may be the reason newer studies are evaluating the benefits of behavioral interventions (Abikoff et al., 2013; Weiss et al., 2012).

The following table summarizes the findings of this study. It compares the numbers of studies that were reviewed regarding each ADHD symptom and the collective conclusions that can be drawn from them (Table 1).

5. Discussion

It is clear that pharmacological interventions are not effective treatments for ADHD with sustained benefits. Stringent criteria are needed for robust comparative studies. The lack of clarity for terms like “long term”, “functioning”, “outcomes”, “academic performance”, “emotional response”, and “normal social interactions” creates ambiguity for researchers, clinicians, patients, and their families. Behavioral interventions lack randomized clinical trials to help determine their effect on core ADHD symptoms. There are many confounding variables that can affect recruitment, retention, data collection, and interpretation. In recruitment, severe ADHD is often found to be associated with anxiety, defiance, and disruptive behavior making it difficult for the researcher to get a pure sample of only ADHD. In patients with mild ADHD the symptoms may not be prominent until later in life when it presents with depression, anxiety, and/or substance abuse. This reduces the likelihood of being able to study the role of psychosocial interventions in lieu of pharmacological interventions. Recognizing milder forms of ADHD is just as important as the more severe forms. Comorbid conditions like ODD and conduct disorder will need to be identified such that

treatment interventions can be tailored to their needs, but also research studies can be better designed. The definition of functioning when addressing the benefits of different forms of treatment is not standardized which makes it difficult to determine effects and benefits.

6. Conclusion

Current evidence suggests that with good compliance stimulants are effective in controlling ADHD symptoms. They are relatively safe and well tolerated for at least 3 years. Short term advantages over other forms of treatment are clear. Neurobiological changes in neuro-imaging do not seem to translate into clinical effectiveness.

More research is needed to evaluate sustained benefits and to study treatment emergent side effects. Although stimulants do not have a sustained therapeutic effect on cessation of treatment, they do not lose efficacy in treatment either. Stimulants seem to minimize the symptoms of ADHD.

Behavioral treatment, on the other hand, lacks long term randomized placebo controlled studies. More recent studies suggest a very promising role for CBT in controlling ADHD symptoms and improving functional, academic, and social outcomes. It does not have the same efficacy as stimulants but has less side effects and better long term cognitive results in adulthood. Also, Inter-therapists variability as well as difficulties that parents may face in ensuring attendance at sessions are some of the challenges that make behavioral interventions more difficult to sustain. CBT is constantly growing with new strategies and methods and may very well prove more effective than thought before. Until more randomized controlled studies are conducted to compare long term efficacy and symptom-specific short-term benefits, the ruling on which form of therapy is best will remain inconclusive.

Table 1
Findings of studies reviewed.

Symptom	# of studies on stimulants effects	Summary of effects	# of studies on behavioral effects	Summary of effects
Academic Performance	4 {(Craig et al., 2015), (Loe and Feldman, 2007), (Zoëga et al., 2012), (Schachar et al., 1997)}	Stimulants improve short-term performance; the ability for patients to “show what they know”.	3 {(Abikoff et al., 2013; Hechtman et al., 2004), (Solanto et al., 2010)}	Behavioral interventions improve homework related performance and academic performance across all subjects.
Executive Functioning/ Organization Skills	2 {(Craig et al., 2015; Vance et al., 2003)}	Mild improvement while on stimulants. Long term benefits are undetermined.	4 {(MTA Cooperative Group, 1999), (Weiss et al., 2012), (Abikoff et al., 2013), (Solanto et al., 2010)}	Behavioral interventions improves long term executive functioning.
Neuro-Biological Effects via MRI imaging	6 {All studies are sited in paragraph 4.1.5 in the article}	Stimulants decrease changes in brain structure when given in therapeutic doses.	None found	No effects have been researched to date.
Functioning & Growth	4 {(Molina et al., 2009), (Harstad et al., 2014), (Craig et al., 2015), (Loe and Feldman, 2007)}	Early improvement is maintained. Overall functioning is lower when compared to normal controls. Long term benefit is not proven.	4 {(MTA Cooperative Group, 1999), (Weiss et al., 2012), (Abikoff et al., 2013), (Solanto et al., 2010)}	Behavioral Therapies improves outcomes in some un-medicated patients. The potential of long term benefits is likely.
Substance Abuse	2 {(Molina et al., 2013), (Wilens et al., 2003)}	The data on stimulants' effect is non-consistent.	None found	Studies that address behavioral interventions' individual effect on substance abuse don't exist at this time.
Long term benefits	4 {(Parker et al., 2013), (Hechtman et al., 2004), (Abikoff et al., 2004), (Shaw et al., 2012)}	No significant improvement after 2 years. Symptoms do not improve. Treatment does not lose efficacy long term. Stimulants merely encapsulate the symptoms.	3 {(MTA Cooperative Group, 1999; Weiss et al., 2012), (Abikoff et al., 2013)}	OTMP symptoms improve with long term treatment. There is data to suggest long term academic improvement. Functioning shows potential in long term benefit.

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