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The long term efficacy of stimulant treatment in executive functioning and emotional regulation in attention-deficit/hyperactivity disorder

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Is a drug efficacious if it is only a quick fix?

Is stimulant treatment efficacious in improving deficits of executive functioning and emotional regulation in order to mitigate predicted poor life outcomes in ADHD?

The long term efficacy of stimulant treatment in executive functioning and emotional regulation in attention-deficit/hyperactivity disorder

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The Division of Science, Mathematics, and Computing

of Bard College

By

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LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

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LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

<table>
<thead>
<tr>
<th>Table of Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title Page</td>
<td>I</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>II</td>
</tr>
<tr>
<td>Table of contents</td>
<td>III</td>
</tr>
<tr>
<td>Abstract</td>
<td>1</td>
</tr>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>ADHD</td>
<td>2</td>
</tr>
<tr>
<td>ADHD Today</td>
<td>7</td>
</tr>
<tr>
<td>Predicted Poor Life Outcomes with ADHD</td>
<td>8</td>
</tr>
<tr>
<td>Treatments</td>
<td>10</td>
</tr>
<tr>
<td>Behavioral Treatment</td>
<td>10</td>
</tr>
<tr>
<td>Stimulant Treatment</td>
<td>10</td>
</tr>
<tr>
<td>Recommended Forms of Treatment</td>
<td>10</td>
</tr>
<tr>
<td>Behavioral Treatment vs. Stimulant Treatment</td>
<td>11</td>
</tr>
<tr>
<td>Stimulant Treatment in the United States</td>
<td>14</td>
</tr>
<tr>
<td>Short Term Efficacy of Stimulant Treatment</td>
<td>15</td>
</tr>
<tr>
<td>Long Term Efficacy of Stimulant Treatment</td>
<td>18</td>
</tr>
<tr>
<td>Executive functioning and Emotional Regulation Deficits</td>
<td>23</td>
</tr>
<tr>
<td>Poor Life Outcomes with These Deficits</td>
<td>23</td>
</tr>
<tr>
<td>Deficits are caused by the symptoms of ADHD</td>
<td>25</td>
</tr>
<tr>
<td>Symptom of Inattention is Underlying Cause of Deficits</td>
<td>26</td>
</tr>
<tr>
<td>Efficacy of Stimulants on Deficits</td>
<td>28</td>
</tr>
</tbody>
</table>
LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

Long Term Efficacy not established with these Deficits ................................. 29

Rationale .................................................................................................................. 31

Rationale for Amphetamines .................................................................................. 33

Amphetamine chemical effect .............................................................................. 33

Amphetamine side effects ...................................................................................... 34

Present Study ............................................................................................................. 35

Procedure .................................................................................................................. 35

Recruitment .............................................................................................................. 37

Screening Day ........................................................................................................... 39

Baseline Measure .................................................................................................... 40

Procedure of Repeated Measures .......................................................................... 40

Predicted Results ...................................................................................................... 44

Data Analysis ............................................................................................................. 44

Main Analyses .......................................................................................................... 45

Discussion ................................................................................................................. 49

Limitations ................................................................................................................ 51

Conclusion ................................................................................................................. 54

References ................................................................................................................. 55

Appendices ................................................................................................................. 68
Abstract

Attention deficit/hyperactivity disorder is a persistent and pervasive lifelong disorder. Children diagnosed with ADHD have poor predicted life outcomes. Specific impairments of inattention are responsible for poor executive functioning and emotional control within the disorder. These deficits are also predictors of poor life outcomes. Stimulant treatment has only been established as an efficacious form of treatment for ADHD in the short term. In order to mitigate the predicted poor life outcomes, stimulants need to be established as efficacious in the long term improvement of psychosocial functioning in ADHD, in order to be considered a truly efficacious treatment. A five year, double blind, placebo controlled, longitudinal study is proposed to address this gap in research. This study will investigate if the benefits of a 24 month amphetamine treatment are sustained three years post treatment. There will be a mixed amphetamine medication treatment group and a placebo control treatment group. The first hypothesis predicts that the amphetamine treatment will reduce the ADHD symptoms in the amphetamine group while they are taking the drug. Secondly, it is predicted that the benefits from the 24 month amphetamine treatment will no longer be present three years after the cessation of treatment. It is expected that stimulant treatment will not mitigate the predicted poor life outcomes in children with ADHD. There should be an increased focus on advancing and promoting alternative treatments other than stimulant medication.
Introduction

ADHD

The Diagnostic and statistical manual of Mental Disorders 5th edition defines attention deficit/hyperactivity disorder as "a persistent pattern of inattention and, or hyperactivity-impulsivity that interferes with functioning or development" (American Psychiatric Association, 2013).

The Development of ADHD

ADHD was not always thought of as an attention deficit disorder, but instead there has been a long development in correctly identifying and characterizing the disorder among children. It has been difficult for researchers and scientists to come up with the definition for ADHD today. Many of the symptoms are homologous with typical child behaviors, and the source of the cognitive malfunctions responsible for these behaviors are difficult to identify. The first reference of children who might fit the current diagnoses for ADHD occurred in 1902, from a report by British physician named George Still (Diller, 1998). He described a group of children he had been studying as “aggressive”, “defiant” “resistant to discipline”, “excessively emotional”, and who showed little “inhibitory volition”. He believed they displayed a “major defect in moral control” and often showed an inclination towards “lawlessness” and “dishonesty”. He considered these abnormalities in their behaviors to be “persistent in their makeup” (Diller, 1998). The descriptions, provided by Still, captured many of the symptoms that characterize ADHD, especially the unremitting nature of the behaviors these children displayed. He, also described other symptoms of emotional and executive dysfunction that children with ADHD often exhibit.
These dysfunctions are the behavioral manifestations of the three symptoms: hyperactivity, inattention, and impulsivity. These symptoms define modern day ADHD. Before Stills’ descriptions of these problematic children came to diagnostic fruition, many other factors were thought to be the cause of these behavioral problems in children with ADHD.

At the start of the twentieth century, the disorder was confused with minimal brain dysfunction. This was due to the spread an epidemic, called of Encephalitis Lethargica, which was characterized by inflammation of the brain due to infection (Lange, 2010). The infection left many people with symptoms of inattention, impulsivity, and hyperactivity (Wodrich, 1994). Children with these symptoms and who had survived the infection were diagnosed with “postencephalitic behavior disorder” (Lange, 2010). It became the norm to diagnose a child with brain damage just from the symptom of hyperactivity alone (Lange, 2010). The attribution of Encephalitis to children, who exhibited this overactive and atypical behavior, contributed to a new and earnest interest in children who were, excessively hyperactive. This furthered exploration and research of hyperactive children and resulted in the subsequent discovery of ADHD (Lange, 2010).

By the 1930s, the disorder was referred to as “restlessness syndrome” (Lange, 2010). Once again, hyperactivity was the most notable symptom and was thought to be the main problem that children suffered from. By the 1940s, there was more recognition of children who had common symptomatology, especially hyperactivity. The causes of the disorder were still attributed to brain injury. Sometimes in more mild cases, behavioral problems were blamed on poor child rearing, or classroom environments that were too lively (Diller, 1998). The rationales
behind the external causes of hyperactivity were due to the widely held acceptance of Freudian thinking and traditional Psychotherapy at the time (Diller, 1998). Even into the 1950’s the symptoms of ADHD were still being recognized as minimal brain dysfunction. There also were some emerging theories that the symptoms were caused by deficits of the central nervous system (Diller, 1998). When the DSM-II came out, in 1968, children with these behaviors were said to have “Hyperkinetic [hyper motor movement] reaction of childhood” (American Psychiatric Association, 1968), with the main symptom still being hyperactivity. This definition led to children being referred to as hyperkinetic or just hyperactive during the 1960s and 1970s (Wodrich, 1994). This same DSM-II definition only listed the diagnosis as a childhood disorder, and was not assumed to extend to adulthood (Wodrich, 1994).

In the 1970s, Virginia Douglas presented her findings from a study at McGill University. She and her team had been observing children for years and had noticed that these children had two other major symptoms, other than hyperactivity. These newly discovered symptoms were inattention and impulsivity. If the child did display hyperactivity, Douglas and her colleagues thought it was due to the deficits in impulse control. The introduction of inattention and impulsivity as part of the disorder marked a turning point, where hyperactivity was no longer the defining symptom of the disorder. Virginia Douglas helped introduce the term, attention-deficit disorder (Diller, 1998; Douglas, 1972). This definition makes an important point; the underlying and main impairment of the disorder is inattention. Douglas and other studies found that hyperactivity was more likely to recede as children grew older, while problems with inattention and impulsivity were more likely to persist past childhood and into adulthood (Diller, 1998; Douglas, 1972). The finding of the persistence of symptoms by Douglas and others gave way to
the idea that ADHD was not just a childhood disorder, but a disorder that could carry on into adulthood. It took a long time to determine the permanent nature of the disorder. This could have been due to the fact that the same outward behaviors and symptoms in childhood ADHD tend to be exhibited differently in adulthood ADHD (Diller, 1998). Original perceptions of ADHD focused on hyperactivity, most likely because it is the symptom that is most outwardly exhibited. The symptom of hyperactivity was also connected with brain damage, which made for an easy explanation for these maladaptive behaviors displayed by children.

The name of Attention-Deficit Disorder officially came out in the third edition of the DSM, in 1980 (American Psychiatric Association, 1980). In the revision of the DSM-III, the term “hyperactivity” was integrated into the definition to make it, Attention-Deficit/Hyperactivity disorder (Lange, 2010). The DSM-III did not list or try to account for possible causes for the disorder, like brain injury or poor child rearing, rather it tried to describe ADHD based on observations of the behaviors and symptoms seen in children (Diller, 1998). This change in approach was particularly important. The basis for identifying and treating the disorder was no longer based in physiology, but rather in behavior. These behaviors would soon be discovered to be the result of cognitive deficits. By the time of the publication of the DSM-III, stimulants had already been introduced into the United States and identified as a successful treatment of children with behavioral disorders. Even though the causes of ADHD were still unknown, treatments were being developed to reduce these maladaptive symptoms. Since a treatment had been found, the focus turned from discovering the causation of the disorder to identifying the behaviors that characterized the disorder in order to make the correct diagnosis.
During the 1990’s, there was a sudden increase in awareness of ADHD and its diagnoses. The eruption of ADHD made an increased demand for treatment. The most fast acting and accessible treatment was stimulant medication. A study by Mark Wolraich, a professor of pediatrics at Vanderbilt University Medical Center, stated that, based on teacher reports, the number of children who “qualified for ADHD raised from 7.3% in the DSM-III to 11.4% in the DSM IV”(Diller, 1998). Based on the revisions that occurred between the two publications, there was a copious increase in the number of children meeting the diagnostic criteria for ADHD. This increase might be seen as unnecessary or dangerous, as it categorized so many children with a behavioral disorder. Many skeptics of ADHD blamed pharmaceutical companies for the increase of the prevalence of the disorder. They were accused of doing so in order to produce higher quantities of their drugs (Diller, 1998). This increase was more likely caused by the new subcategories added into the DSM-IV, of inattentive type, impulsive-hyperactive type, or combined, where both symptoms are present (Lahey et al., 1994 & Lange, 2010). This categorization highlights the different ways ADHD manifests itself. It also highlights inattention as being the core feature of the disorder, not hyperactivity. Wide public recognition from the DSM-III, of the disorder, as well as pre diagnostic questionnaires such as the Conner’s rating scale, were being widely circulated and produced at an increasing rate. This contributed to an increase in diagnoses (Schwarz, 2016). There were many who were hesitant towards the accepted growth in the diagnosis of ADHD and stimulant treatment in the 1990s. Despite this resistance, ADHD was becoming the most common childhood disorder, and still is today. The significance in the history of ADHD, and its sudden increase, raises the question of how to effectively address and treat it.
ADHD Today

Diagnosing children with ADHD is much more complex than just following a checklist of behavioral symptoms. The DSM-5 states that these symptoms must occur to a degree that they are developmentally inappropriate, and have persisted for at least six months (American Psychiatric Association, 2013). These symptoms must cause a significant difficulty for the child in at least two realms of their life: home and school. For adults, this realm includes their workplace (American Psychiatric Association, 2013). These symptoms must cause crucial impairments in the functioning of the child, and create maladaptive behaviors in specific areas of their life. Meaning the disorder has detrimental effects on their development and functioning. These problems, deficits, and behaviors cannot be better explained by some other disorder (American Psychiatric Association, 2013). The exact causes of ADHD are still disputed and largely unknown. ADHD is known to have a genetic component, considering it has been proven to run in families (CHADD, 2015). This genetic component is a factor to take into consideration in the process of diagnosis and treatment.

ADHD is one of the most common behavioral conditions, affecting around 11% of school aged children (Visser et al., 2014). ADHD typically emerges in preschool children around the age of three or four (Mayes et al., 2003). Often thought of as only a childhood behavioral condition, which is unfounded. 75% of children who are diagnosed with ADHD continue to exhibit symptoms into adulthood (Brown, 2013). By the age of fifteen, 75% of adolescents with the diagnosis of childhood ADHD continued to meet the DSM-5 criteria for the disorder (Molina et al., 2003). The behaviors of hyperactivity have been shown to lessen overtime, while
inattention and impulsivity tend to persist to adulthood (CHADD, 2015; Douglas, 1972). Long term studies have demonstrated that ADHD is not a disorder that children “outgrow”. Symptoms tend to pervade through adolescence and adulthood (Mayes et al., 2003). Adults who have ADHD often have chronic feelings of embarrassment, frustration, and oftentimes failure. This is because they struggle with day to day tasks, have problems in their relationships, and have trouble completing long term goals (CHADD, 2015). Considering that the disorder is lifelong, it often has long term negative effects on the lives of people who suffer from it.

**Predicted Poor Lifelong Outcomes with ADHD**

In longitudinal studies, ADHD diagnosis has been found to be a strong predictor of poor psychosocial functioning in adulthood (Rasmussen, 2000). Children with ADHD also show poor educational and academic outcomes. ADHD diagnosis has been linked to “poor grades, low standardized test scores, expulsion, as well as low rates of high school graduation, and of postsecondary education, compared to non ADHD controls” (Loe & Feldman, 2007). Matched controls refer to non ADHD patients that had similar demographic backgrounds as the ADHD patients. These poor life outcomes can also be attributed the symptoms of ADHD, which cause poor executive functioning and poor emotional regulation in people with the disorder (Barkley, 1997; Barkley, 2001; Barkley 2010). The poor prognosis of life outcomes for children with ADHD is important in establishing lasting effective and sustainable treatments. These treatments should be able to normalize coping tools and should be integrated into an individual's daily functioning.

The symptoms that adults with ADHD most commonly exhibit include “inattention,
distractibility, lack of organizational skills, and problems completing tasks efficiently” (Spencer et al., 2007). All of these symptoms, which are reminiscent of developmentally inappropriate functioning, are instrumental in “academic or occupational failures” (Spencer et al., 2007). In studies investigating ADHD in adults and their non ADHD siblings, siblings with ADHD had more work tribulations, a higher likelihood of switching jobs, lower rates of educational achievement, and an overall lower socioeconomic status compared to their non ADHD siblings (Spencer et al., 2007). When compared with non ADHD controls, people with ADHD have also been shown to have fewer social connections, poor social adjustment, as well as a higher propensity towards substance abuse (Spencer et al., 2007). The cognitive impairments that result in poor daily functioning in childhood ADHD result in poor life outcomes in adulthood. These cognitive impairments are not just predictive of academic handicap or failure, but are also predictive of overall life successes or failures due to the importance executive functioning and emotional regulation have in all different domains in life.

The symptoms of ADHD have all-encompassing effects on the lives of people affected by the disorder. It is imperative to understand the neurocognitive functions that cause these symptoms, which in turn cause maladaptive behaviors, for effective treatment methods (Wang et al., 2015). Academic performance is not the only area affected. These cognitive impairments debilitate other functions such as inhibition, shifting, and attentional resources (Mischel, 1989; Barkley; 1997; Barkley, 2001; Mahone et al., 2002), which affect parts of functioning other than just academic. This means treatments need to address the sectors of social, emotional, and general efficiency within people’s lives. These are predictors of lifelong outcomes as well.
Treatments

**Behavioral Treatment.** Behavioral therapy consists of many different interventions. These interventions usually consist of regular meetings with a therapist for both, the child, and the parents. Parent training occurs with a therapist in order to understand how to correct maladaptive behaviors their child exhibits. School services are often employed to help the child with academic concentration (Center for Disease Control and Prevention, 2017). These behavioral therapies are thorough and effective.

**Stimulant Treatment.** Stimulant treatment can consist of many different medications. The first of the most commonly prescribed medications is mixed amphetamine, also known as Adderall. The second of the two most commonly prescribed medications is methylphenidate, also known as Ritalin or Concerta (CHADD, 2017). When children are diagnosed with ADHD, either a pediatrician or psychiatrist can prescribe them a dosage of the medication. They can check back in every three to six months for an adjustment of medication, and to evaluate individual effects of medication (Center for Disease Control and Prevention, 2017).

**Recommended Forms of Treatment.** Numerous studies confirm that the combination of behavioral treatment and stimulant treatment is more efficacious than either treatment alone (Smith & Shapiro, 2006). This research is substantiated by the fact that both The Center for Disease Control and Prevention and the American Psychiatric Association, recommend combined treatment as well. They recommend that the combination of behavioral therapy and stimulant treatment are superior to administering just one form of treatment, or no treatment at all (CDC & APA, 2016). The CDC advises that for younger children, behavioral therapy should
be the first form of treatment. Medication should be secondary to behavioral therapy (2017).

**Behavioral Treatment vs. Stimulant Treatment.** Despite the professional recommendation that behavioral therapy be the primary form of treatment, with medication being secondary, this is often not what occurs when a child is diagnosed. More than half of the children diagnosed with ADHD are being treated with stimulants (CDC, 2016). While the prescription of stimulants continues to rise, populations most affected include areas of lower socioeconomic status, as well as areas that are more rural (NIMH, 2016).

Behavioral therapy entails a set of interventions that involve constant child, parent, teacher, and therapist involvement. This form of treatment requires a substantial amount of resources such as money, time, attention, and energy. A prescription of stimulants requires one consultation, with a few follow up consultations to adjust dosage. This stimulant treatment does not require nearly the same amount of resources that behavioral therapy does. There are many benefits behavioral therapy offers, that medication does not. For example parent training. This helps parents teach their children correct social and sharing skills, which are essential for development. Learning proper sharing skills could help children understand reciprocation and prosocial behavior. These acquired skills could help them in the future when working in a team, or office. Often behavioral therapy is an afterthought. Medication is used as the first line of treatment. Unfortunately, medication is thought to be the answer to all behavioral problems.

An ADHD diagnosis puts an incredible burden on the family, or those directly involved with the individual diagnosed. Results from a study evaluating the financial burden of medical expenses, direct cost, work loss, and indirect cost, of family members and individuals with the
disorder found that:

“The annual average expenditure (direct cost) per ADHD patient was $1,574, compared to $541 among matched controls. The annual average payment (direct plus indirect cost) per family member was $2,728 for non-ADHD family members of ADHD patients versus $1,440 for family members of matched controls “(Swensen et al., 2003).

Other difficulties families might have is transportation, convenience of location, and awareness of other tools other than medication for children with ADHD. A map of the United States demonstrates how North Dakota, Wyoming, Nebraska, Kansas, Iowa, Missouri, Wisconsin, Indiana, Louisiana, Alabama, North Carolina, and Tennessee all have a high concentrations of children being treated with medication. These states have more rural landscapes, and lower incomes in these areas (U.S census Bureau, 2016). While other states who have lower concentrations still have the population of children being treated with medication at or less than 65%, which is still a very large percentage of children being treated with medication.
Figure 1. State prevalence of children with ADHD diagnosis taking medication. States with more rural makeups have a higher population of children taking medication for ADHD (Division of Human Development and Disability, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, 2011).

Co-author Benedetto Vitiello, M.D., of NIH’s National Institute of Mental Health stated that "stimulant medications work well to control ADHD symptoms, but they are only one method of treatment for the condition. Experts estimate that about 60 percent of children with ADHD are treated with medication," (2011). The CDC’s statistics from 2009 to 2010 found that:

“less than 1 in 3 children with ADHD received both medication treatment and behavior therapy, the preferred treatment approach for children ages 6 and older, while half of preschoolers were taking medication for ADHD” (APA, 2011).

The CDC has reported that stimulants are the most prominent and commonly used medication in ADHD treatment. This is backed by the significant finding that approximately 70% to 80% of children who take stimulants have a reduction in ADHD symptoms (CDC, 2016).
Despite the recommendation of combined treatment, stimulant treatment is cheaper and acts faster than behavioral therapy. It is also used as the first and more common form of treatment, and is thought of as a cure for ADHD.

Stimulant Treatment in The United States

Since Charles Bradley found that the stimulant Benzedrine helped subdue misbehaved children in 1937 stimulants have been used to treat childhood ADHD for 80 years (Strohl, 2011). Methylphenidate was first brought into the United States in 1955 and then approved by the Food and Drug Administration in 1961 (Chiarello, 1987). The largest growth of stimulant pharmacotherapy, as well as ADHD diagnoses, occurred in the 1990s. During this time, the amount of physician visits for stimulant treatment increased five times from what they had been before (Mayes et al., 2008). The enormous increase in the diagnoses of ADHD and stimulant treatment led to an immense amount of resistance and suspicion about stimulant treatment for children with ADHD.

In reality, the large increase of stimulant prescriptions to meet the rapidly growing diagnoses was caused by some crucial changes in government policy, and public education. Firstly, the Supplemental Security Income program was modified by the Supreme Court to include low income children diagnosed with ADHD. This meant they were finally able to receive the benefits of the program like providing stipends for medication (Mayes et al. 2008). Secondly, from the outcry of parents of children with ADHD, the Individuals with Disabilities Education Act was changed by congress to include ADHD as a disability that would be protected (Mayes et al. 2008). This resulted in children being able to have special accommodations on tests,
LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

homework, and other school activities. Finally in the 1990s, Congress increased the amount of people eligible for Medicaid, especially for children. This would cover medication but not necessarily therapy (Mayes et al. 2008). These events contributed to the present climate of ADHD culture in the United States. As of 2008, 8% of children from the ages four to 17 were diagnosed with ADHD. Roughly about 4.5% of those diagnosed were using stimulant treatment. That means that by the early 2000s, stimulant medication was the most commonly used form treatment for children with ADHD.

Of the entire world’s production of stimulants, children in the United States consume the majority (Mayes et al., 2008). The efficacy of stimulants did not lead to prescription increase, but was rather driven by certain social and political factors. The majority of diagnoses and stimulant prescriptions are made by primary care physicians of children in the United States (Zito et al., 1999). Psychiatrists can also prescribe the stimulant medications to children with ADHD. Interestingly, the prescription of medication for children varies around the world. In some European countries only a child psychiatrist can prescribe stimulants to a minor. In others, a child can only receive stimulant treatment if approved by three separate professionals (Mayes et al., 2008). This history of stimulants, how they rose to popularity for the treatment of ADHD, and are still popular in the United States today, contributes to the explicit understanding of the use for stimulant medication as a first form of treatment for children with ADHD.

Short Term Efficacy of Stimulant Treatment

There is still much debate on whether or not stimulants are the best line of treatment. Arguments for stimulant treatment often cite the immediate improvement and change brought on
by the drug. Thus, rendering it extremely effective. Studies have demonstrated that stimulant treatment is highly effective for people with ADHD (Spencer et al., 2001; Spencer et al., 1996; Garland, 1998). Through data collection and research, stimulants have been shown to have short and intermediate term efficacy in the reduction of symptoms of ADHD (Garland, 1998).

Both Adderall and Ritalin have been shown to be more effective treatments for ADHD in children and adults, as compared to a placebo method (Manos et al., 1999; Spencer et al., 2000). A study conducted by Manos and colleagues revealed that, all children on either Adderall or Ritalin had a reduction in behavioral symptoms, compared to the children in the placebo control group (1999). Both medications are more efficacious than no treatment at all; this had been established relatively early in stimulant research (Spencer et al., 2000). These results are based off of teacher, parent, and clinician reports using the Conner’s Teacher rating scale, as well as The Global Impression Scale (Spencer et al., 2000). It can be established that stimulants are efficacious for children with ADHD, compared to no treatment at all. These results also corroborate the notion that stimulants are effective in reducing the problematic behavior and academic difficulties.

Stimulant use seems to be efficacious in the short term for academic performance in areas such as completed work, and better performance on math tasks. Yet other evidence suggests that the long term effectiveness of stimulants does not account for academic attainment, such as “education level, grade point average, and withdrawal from classes” (Baroni & Castellanos, 2015). For example, one study measured the efficacy of methylphenidate and Adderall in school aged children in an effort to expose which type of deficits the medication improved. They used
The School Situations Questionnaire-Revised as one of their measures to decipher school performance improvement in the medication treatment group. This measure consisted of questions for teachers which addressed the problems with attention and concentration on school related activities in children with ADHD (Manos et al., 1999). At the end of the study, stimulants proved to be a viable and effective treatment option in the reduction of ADHD symptomatology. They proved to be efficacious with continued use and with short and intermediate term benefits. Certain executive functions were improved such as children’s organizational skills. This was only demonstrated throughout the stimulant ingestion period. Once again, there is little to no evidence demonstrating long term superior executive functioning. Thus, this area requires further research (Craig et al., 2015).

It seems that stimulants manifest their effect mostly in academic performance of children. This also might be the main motivator for families to give their children medication. What parents do not know is that stimulants are only responsible for short term academic successes. They show no evidence of contributing to improved long term academic attainment and performance (Craig et al., 2015). Long term improvement is unclear. Some studies often refer to stimulants as aids for children to “show what they know”, rather than increasing their prospects of learning or gaining effective study or coping mechanisms which would help academic performance throughout their lifetimes (Craig et al., 2015). Stimulants have been correlated with improvement in “note taking, test taking ability, concentration, listening” (Zoega et al., 2012), as well as “homework completion and written language output” (Evans et al., 2001). However, these academic improvements are not habitualized or sustained with stimulant usage. One study perfectly captured the essence of stimulants and what they lack: “stimulants, unlike learned
behaviors, cannot be applied to the discipline of learning coping mechanisms, and used to implement this gained knowledge overtime” (Rapport et al., 1994). Stimulants are not a tool or skill that one can use throughout their lives, but rather a short term solution to a long term problem. In contrast, another study provides evidence of improvement that is maintained for 2 years. Importantly, this was only possible with continuous stimulant treatment (Schachar et al., 1997). Many findings are conflicting, and add more complexity to the real world efficacy of stimulants for people with ADHD. Complexities of stimulant usage and prescription need to be defined by whether or not the short term improvements can be applied to the long term outcomes.

**Long Term Efficacy of Stimulant Treatment**

Despite the overwhelming substantiation of ADHD symptom reduction with stimulant treatment in the short term, there has been a lack of sufficient evidence for the efficacy of stimulant treatment is in the long term. There has been considerable demand for more long term research with stimulants. This need for research is to verify the long term safety of stimulants and its effects on the human body. There has also been a demand for a redirection in research, which should investigate whether or not those who take stimulant medication are able to make habit of their changed behaviors, once no longer on the drug. This long term research is necessary to establish if, stimulants make these daily adaptive behaviors into enduring characteristics. If these adaptive behaviors are sustained, it could help people with ADHD ascertain lifelong outcomes similar to those without the disorder.

Even though there is a gap in longitudinal research for stimulants (Jureidini 1996), there
have been longitudinal studies that have tried to address long term efficacy stimulants. The enduring effects of stimulants are still unknown. As is whether or not long term functioning is improved or unaffected (Mcgough et al., 2005). Studies have been conducted in an effort to substantiate the robust efficacy of stimulants.

Mcgough and colleagues conducted a 24 month open label extension of two placebo controlled studies, which had forty five research sites. Children who had been in a six week double blind placebo controlled study were chosen for long term treatment, and in the Mcgough study were given a continued dosage of Adderall. They used teacher and caregiver assessments of the Conner’s Global Index Scale, to operationalize their variable of ADHD symptoms. This was a naturalistic study, meaning, children were observed naturally in their normal home and school settings, without completing specific laboratory tasks or tests. In order to test the long term effect of this drug, the researchers collected baseline measurements that were compared to measurements taken every three months after. In order to see whether or not, or by how much the Adderall dosage was improving the children’s symptoms at each time of measurement compared to the baseline measurement. Their treatment groups consisted of one group which was treated in the previous study and had discontinued treatment in between the current study and the previous one, a second group that received placebo in the previous study but received treatment in the current study, and lastly a third group, who had continuous treatment throughout both studies. All participants showed overall improvement throughout the duration of treatment in the Mcgough study regardless of treatment group (Mcgough et al., 2005). But those who had uninterrupted treatment had longer and more significant improvement than the other two groups. Children who had sustained treatment for over two years showed more improvements in their
LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

...daily lives. This points to the necessity for establishing if these improvements from long stimulant treatment will be maintained, after the long term treatment is no longer being administered.

The Mcgough study is an example of a good starting point for longitudinal research in treatments for children with ADHD. After the quarterly measurements for their different treatment groups, the study did not have a post treatment measurement for all of the participants. A study where there is continuous evaluation after cessation of treatment at multiple life milestones could help ascertain at which time point stimulants no longer make a difference. Having another evaluation towards the end of life could help establish whether stimulants make a difference in the poor life outcomes for people with ADHD. This study does demonstrate long term efficacy throughout the duration of treatment, but nothing further. This does not advance research as to whether or not stimulant treatment makes a positive difference in the long term. The Multimodal Treatment Study (MTA) has established that 14 month stimulant treatment has been effective. Their findings also concluded that ongoing administration of stimulants is necessary for continuation of long term improvement (Vitiello et al., 2001).Now that long term treatment has been established in the interim of stimulant medication, it is imperative to establish if it is still efficacious post treatment. If the improvements are maintained, they will be predictive of functioning in subsequent years.

Even though ADHD is persistent to adulthood in most individuals, one distinguishing and common feature of ADHD treatment is that medication is discontinued, this discontinuation especially occurs during adolescence or early adulthood. The importance of treatment
discontinuation for long term outcomes is largely unknown (Lichtenstein et al., 2012). At the eight year follow up measurement in the MTA study, 61.5% of the participants taking the medication treatment had stopped taking their medication. This is a large percentage of patients to completely terminate their treatment method, for a pervasive and persistent disorder (Molina et al., 2009). There is also evidence that there is a severe drop in medication adherence in adolescence, while the disorder is still present (Molina et al., 2009). If patients stop taking their medication then the medication must be efficacious post treatment in order to improve negative life outcomes.

In the same MTA study, the medication group showed improvement in functioning at the 14 and 24 month follow ups. At the later assessments, this treatment group was found to have worse functioning and more school services. One exception to this functioning is that they still improved on the math performance test at the 36 month follow up (Molina et al., 2009). Other studies have found evidence for prolonged improvements in ADHD symptoms three years post treatment, but after three years the benefits of the one time 14 month stimulant trial are no longer present in participants (Craig et al., 2015; Murray et al., 2008). After the six and eight year follow ups, the improvements from stimulants are no longer present. This data fails to provide support for the long term efficacy of medication treatment. It cannot be extended beyond the short term reduction of symptoms throughout the duration of medication administration (Molina et al., 2009). The MTA states future research should focus on treatments that targets specific impairments, instead of just ADHD symptoms. This could help establish new treatment methods that would be more likely mediate adulthood functioning (Molina et al., 2009). This MTA study suggests that the approaches to treatment methods should be changed, in hopes of improving
them. Before research is allocated to new direction, the scientific community must establish that stimulants are not the most efficacious treatment. Using stimulants as the only form of treatment could be harmful to children. It could prevent them from getting treatment that could benefit them for the entirety of their lives. This would be most successfully accomplished by long term testing of stimulant treatment. Doing so would involve measuring specific impairments in ADHD, which are also predictive of long term functioning, and see if there is long term improvements, after prolonged treatment with stimulant medication.

There has not been a sufficient amount of evidence of long term positive life outcomes for ADHD children treated with stimulants. This is despite the well documented improvement in life quality during stimulant treatment (Rajeh et al., 2017). There is much more evidence supporting the short term advantageous symptom reduction due to stimulant treatment compared to the long term outcomes of stimulant treatment. This lack of evidence does not necessarily indicate that stimulants have no long term benefits. Rather, there have not been enough studies to substantiate possible beneficial impact in the long term. Although, there is evidence of children being able to perform significantly better in an academic setting while using the medication. Yet they are incapable of applying these improvements or developed skills after the treatment is discontinued. This finding demonstrates that stimulants can aid in the reduction in ADHD symptoms in children. Yet they do not assist in the development of imperative skills that could help children establish enduring coping mechanisms for future life events. There needs to be more longitudinal research in order to establish long term efficacy for stimulants in children with ADHD, that lasts into adulthood.
Executive functioning and Emotional Regulation Deficits

Poor Life Outcomes with These Deficits. Executive functions are a chain of cognitive processes. They involve impulse control and attentional skills that are essential for daily activities. These skills include things like planning and organization. Emotional regulation is the ability to appropriately inhibit or alter emotions to fit the context of a situation. When poor emotional regulation occurs, it is thought to be a product of impaired executive functioning (Barkley, 2010). Deficits in executive functioning and emotional regulation are thought to be especially predictive functions of an individual. These affect their long term performance (Sobanski et al., 2010). These deficits are thought to be predictive of life outcomes because they help people adapt to and cope with new situations. They also assist people with troubleshooting: “working memory, problem solving, predicting outcomes, oscillating between tasks, and being able to control overt and negative emotions” (Barkley, 2010). People, who have poor emotional regulation often display behaviors that fluctuate in emotions while in inappropriate or inconvenient situations.

An emotional regulation deficit is one of the most obvious manifestations of impairments in executive functioning. Subsequently, there is more evidence of emotional regulation being correlated with poor life outcomes. Studies have found that poor emotional regulation in individuals, has contributed to:

“higher rates of incarceration, worse academic achievement, higher incidence of driving accidents, and more malfunctions in social and marital relationships than those who did not show large levels of emotional lability” (Barkley, 2010).

One of Barkley's studies demonstrated that poor emotional regulation had a larger effect on individual's overall functioning and impairment, than hyperactive or impulsive symptoms did.
This demonstrates that poor executive functions have a greater effect on a person’s impairment than other symptoms of ADHD. The long term significance of poor emotional regulation becomes clear in extreme emotional lability in youth. This has been shown to predict poor adult psychosocial functioning up to twenty years later (Stringaris et al., 2009).

Deficits in executive functioning and emotional regulation contribute to poor life outcomes in people with ADHD. ADHD is often associated with a negative impact on social functioning. Children who have ADHD can be troubled with peer rejection and have weakened peer relationships (Mash & Barkley, 2003; MTA, 1999; Maoz et al., 2014). Poor emotional regulation predicts more peer rejection and negative social outcomes for those who have been diagnosed with ADHD (Sobanski et al., 2010). These deficiencies in the ability to maintain proper social interactions and relationships could be a predictor of negative life outcomes for children diagnosed with ADHD. The inability to properly communicate and inhibit could be the repercussion of poor emotional regulation in children with ADHD (Maoz et al., 2014). Since poor emotional regulation and executive functioning are already connected with poor life outcomes. It could be assumed that these impairments in people with ADHD account for some of the poor life outcomes in the ADHD community.

Many studies point out the need for real world measurements of executive functions. Considering these functions exhibit themselves in everyday life, like social interactions and efficiency studies should try to quantify these daily functions. Laboratory tasks, fail to produce results that are applicable to real world functions and emotions (Jarrett, 2016). Jarrett found that self-reported executive functioning deficits were most strongly related to inattention and less
related to hyperactivity and impulsivity. At the conclusion of the Jarrett study, a need for future was expressed that addressed emotional regulation in real world aspects of life. Since it is also associated with negative life outcomes finding accurate measurement tools is crucial.

**Deficits are caused by the symptoms of ADHD.** Emotional dysregulation has reemerged as an associated impairing symptom of ADHD, in children and adults (Skirrow, 2014; Sobanski, 2010). The Dyscontrol Theory attributes poor emotional regulation to deficits in executive functions, in children with ADHD (Barkley, 1997). This demonstrates that poor emotional regulation is accountable for the inability to inhibit responses provoked by emotional stimuli (Barkley, 1997). According to this theory, children are usually capable of normal emotional behavior. Yet children with ADHD, have difficulty with inhibition, which is caused by their impulsivity. This lack of inhibition manifests itself in deficits in executive functions, which then creates poor control of emotions (Posner et al., 2014). This deficit in emotional regulation is the inability to divert attention away from overly negative emotions, and adapt correctly to the current situation. Problems in executive functioning and emotional regulation could be attributed to impairments in executive inhibitory control (Barkley 1997). Impulsivity is thought to be caused by inattention (Mischel, 1989). This means that inattention contributes to the deficits in executive functioning and emotional regulation. These deficits have direct effects on daily functioning and long lasting effects on later life outcomes for people with ADHD.

This theory views poor emotional regulation as a behavioral manifestation of impaired executive functioning, which is seen as a product of inattention. Meaning that poor emotional regulation and impairments in executive functioning are caused by impulsivity and disinhibition,
which is the consequence of inattention (Posner et al., 2014). Inattention and impulsiveness are the two main persistent symptoms of ADHD that carry on into adulthood (Sobanski et al., 2010). This means without intervention, impairments of executive functioning and emotional regulation will persist through adulthood.

**Inattention is the underlying cause of These Deficits.** Impulsivity manifests itself through disinhibition which is caused by malfunctions in attentional abilities (Mischel et al., 1989). In an early study conducted by Walter Mischel, researchers demonstrated that certain preschooler’s inability to inhibit or delay gratification was predictive of their behavior ten years later (1989). Children who waited longer for a reward were reported to be more academically and socially well off compared to their peers. An inability to self-regulate attention in childhood was shown to be predictive of problems with “resilience, antisocial behavior, low social responsibility, and difficulties with conduct” (Mischel et al., 1989).

In the study there was a series of manipulations for children to either immediately receive a reward of small value or wait for an extended amount of time for a more desirable reward. To manage their self-control and inhibit immediate gratification children had to control their attentional skills. This self-control was in the pursuit of a better reward in the long term. It seemed that children had to direct their attention elsewhere other than the desired object. Children who directed their thoughts to other “distracting” thoughts or thought of the reward in an abstract way, increased their waiting time for the reward. The children who were able to control and direct their attentional skills in this manner, showed a higher propensity for the pursuance of long term goals rather than immediate gratification (Mischel et al., 1989).
A study examined alcohol use and executive functioning amongst college students with ADHD. They found that students with ADHD have more alcohol related impairments than their non ADHD peers (Langberg et al., 2015). Interestingly ADHD college students do not statistically drink as much or as often as their peers but have greater impairments. Researchers thought that deficits in executive functioning could play a mediatory role in these real world impairments that are manifested through alcohol use. Students with ADHD were not able to obtain the same level GPA as their non ADHD peers, because they were giving into alcohol consumption at times that inhibited them from completing their school work (Langberg et al., 2015). The role executive functions play in the achievement of long term goals is crucial. These executive functions are necessary to ensure that ADHD students do not always give into immediately gratifying activities like drinking. In order for them to keep up with school work and make long term success in college come to fruition. If these ADHD students actively tried to redirect their attention away from desirable stimuli (alcohol), they might achieve higher GPAs in college. Alcohol was shown to negatively impact the motivations of college students with ADHD to pursue long term goals in the face of immediate gratification. This ultimately results in more negative overall outcomes. For example, graduation rates (Langberg et al., 2015). These findings are similar to how children who had more self-control and inhibited immediate gratification had better life functioning. As opposed to children who acted impulsively and took the immediate and lesser reward and had impairments in functioning later in life (Mischel et al., 1989).

Inattention is at the basis of the deficits of executive functioning, and emotional regulation. Attentional abilities dictate inhibition, impulsivity, and motivation. Furthermore,
there is evidence that children with ADHD often exhibit difficulties in peer relationships because they do not have the correct empathetic responding (Cordier et al., 2009). This is not because they are naturally deviant or unfeeling. Instead, it can be explained by their attentional impairments. These affect them being able to properly attend to pertinent stimuli, such as “facial expressions, or minute actions, outside themselves” (Cordier et al., 2009).

Deficits in executive functioning and emotional regulation are caused by inattention. Executive functions help maintain and control behavior, more specifically goal directed behavior (Bron et al., 2014). Evidence that impairments in emotional regulation and executive functioning are present in ADHD have been verified in multiple longitudinal studies (Sobanski et al., 2010 & Strine et al., 2006). Constant inattention in ADHD is responsible for this poor inhibition. This poor inhibition is responsible for the impairments in “goal directed” behavior and the impairments in emotional regulation (Barkley, 1997). Since inattention is the main cause of these deficiencies, more focus needs to be allocated to how children can develop affective attentional skills to help them accomplish their goals.

**Efficacy of Stimulants on These Deficits**

It is still very controversial whether or not administration of stimulants improves long term cognitive functions in patients with ADHD (Wang et al., 2015). In a study with a 24 month treatment period of methylphenidate only symptoms of impulsivity and disinhibition improved in the long term treatment of stimulants, but not symptoms of inattention (Wang et al., 2015). The findings from this study were hard to interpret since their study was longitudinal they could not tell if the improvement was from the medication, maturation, or improvement from practice on
repeated measures. They concluded that more research is needed in order to establish whether or not stimulant treatment can change and sustain cognitive functions throughout a lifetime (Wang et al., 2015).

Stimulants are associated with better outcomes such as “higher self-ratings of well being and social adjustment” (Baroni & Castellanos, 2015). The improvement in simulated or real driving due to stimulant treatment might be the result of improved emotional regulation and sustained attention (Advokat, 2013), meaning that stimulants might have more benefits than just improvements in academic performance. A twenty four weeks study found that MPH improved emotional dysregulation and mood regulation (Rosler et al., 2010). A pilot study was conducted where children with ADHD who were treated with MPH, which improved their performance on tasks of empathic responding and the ability to interpret verbal and facial cues (Maoz et al., 2014). Students have reported that stimulants not only affect their cognition but also their emotional and motivational states (Baroni & Castellanos 2015). Future research should include what benefits long term stimulant use can produce other than classic neurocognitive performance, but rather other domains such as emotional regulation and executive functions that could be mediators to real world lifelong outcomes (Baroni & Castellanos 2015). There is still a large gap in research of long term stimulant efficacy of improving attentional functions of executive and emotional control that predict maladaptive behaviors.

**Long Term Efficacy not established with these Deficits**

It has been confirmed that stimulants help diminish the number of negative social and peer interactions in children with ADHD. They have also been shown to help social and
behavioral functions in children with ADHD (Maoz et al., 2014; Bagwell et al., 2001).

Methylphenidate has been shown to improve executive functioning deficits that are connected to “attention, vigilance, response time, as well as inhibition in children” (Bron et al., 2014).

Methylphenidate has been proven as an effective form of treatment that helps children improve in goal directed tasks that are associated with deficits in executive functions (Bron et al., 2014). Stimulants are beneficial to the deficiencies in executive functioning which might help to control the maladaptive emotional behaviors in people with ADHD (Posner et al., 2014). In one study, patients that had previous criminal convictions, who received stimulant treatment had a reduction in criminal activity. Crimes occurred less often during the periods they consumed stimulant medication. Meaning that medication reduced their risk for criminality among patients with ADHD (Lichtenstein, et al., 2012). The researchers also looked into the long term effects of this medication in relation to criminality. They looked at rates of criminality from 2006 to 2009. There was no significant relation before administration of medication use in 2006 or after cessation of medication in 2009. This means that there was no significant decrease in crime rate after patients terminated treatment with medication. The medication was efficacious only during active treatment and did not benefit these convicts in the long run. This finding is significant because, there is only evidence short term efficacy of stimulants for improvement in executive functioning and emotional regulation (Lichtenstein et al., 2012).

Not that much empirical support for the effects of stimulants on emotional regulation or executive functions is distinct from short term efficacy of stimulants on ADHD in general (Posner et al., 2014). There have been a couple randomized double blind, placebo-controlled trials of stimulant treatment on children and adults which have shown that stimulants do reduce
emotional dysregulation. In fact significant decreases in poor emotional regulation were found through parent and teachers’ ratings of children's behaviors (Coghill et al., 2007). Long term follow up studies are necessary in order to, decipher if stimulants are responsible for reductions in poor emotional regulation and executive functioning. Additionally if the negative outcomes connected with ADHD are reduced in the long term by reducing these deficiencies (Posner et al., 2014). It is imperative to establish if stimulant treatment still has beneficial effects on patients executive functioning after cessation of treatment, not just in the duration of treatment.

**Rationale**

In evaluating the current body of literature, it is clear that ADHD is a persistent set of symptoms that affects life outcomes. Given this finding, it is necessary to decipher the efficacy of long term stimulant treatment. ADHD and its symptoms can have negative effects on an individual’s life outcomes. It is important to invest further research into the abiding efficacy of long term treatments. The reality is that many children are medicated as a first form of treatment. Instead of following the guidelines of the CDC to treat symptoms of ADHD with a combination of behavioral therapy, school interventions, and medications if needed. Taking into account the reality of stimulant usage for children with ADHD, more research is necessary in order to establish that stimulant treatment is capable of reducing enduring symptoms of ADHD. Thereby, creating habits of adaptability in people with ADHD, to make significant lifelong effects.

Considering, the short-term efficacy of stimulants have been established in the reduction of ADHD symptom, and improvements in daily tasks, one would hope that these findings would be applicable to the long term outcomes of people who use stimulant treatments. If stimulant
treatment is only useful in the short term, this would make a dependence on the medication, and not let people with ADHD be able to develop adaptable coping skills to address their symptoms that, cause deficits in their functioning.

Specific deficits such as executive functioning and emotional regulation that are predictive of poor life outcomes are products of ADHD. The deficits of executive functioning and poor emotional control are poor lifelong predictors for people without ADHD, as well as people with the disorder. These deficits are predictive of the life outcomes of people regardless of the disorder being present. This demonstrates their importance in all human functioning. Stimulants have been proven to lessen the impairments in these deficits in people with ADHD. But only while actively consuming the medication. It is important to establish that stimulants are able to have lasting positive effects on these impairments, so that people with ADHD can have improved lifelong outcomes.

Long term stimulant efficacy either needs to be established or proven incapable sustaining its effects. In order to see whether future research should be directed in either advancing stimulant treatments or focusing on alternative treatments. This study asks whether or not stimulants will persist in their efficacy in the long term. This will be measured by the long term symptom reduction of executive functioning and emotional regulation after cessation of the treatment. If executive functioning and emotional regulation are improved even after the cessation of treatment, it would be assumed that those individuals would have improved life outcomes compared to those who received no treatment at all.
Rationale for Amphetamines

Amphetamines are a type of stimulant that are used to treat people with ADHD. The most commonly prescribed amphetamine for children with ADHD is a mixture of amphetamine and dextroamphetamine salts, also known as Adderall (NIDA, 2014). This type of stimulant will be used in this study as opposed to other types of stimulants based on previous studies that have found this amphetamine treatment as the most efficacious and to have the least amount of negative side effects (Faroane et al., 2001 & Faraone & Buitelaar, 2010).

Amphetamine chemical effect

Amphetamines have a significant effect on the brain and its neurotransmitters. Amphetamines increase the presence of the neurotransmitters dopamine, epinephrine, also known as adrenaline, and norepinephrine, which are called Catecholamines. These neurotransmitters all serve different functions in the body. Dopamine contributes to the function of the central nervous system. It plays a role in attention, learning, movement, as well as other behaviors. Norepinephrine and Epinephrine are incidental to the fight or flight response in the body. They increase heart rate by releasing glucose and allocating blood flow. This ensures that the body is ready for active movement (Schacter et al., 2011). Amphetamines have a similar structure to a catecholamine. Which enables them to enter the terminal of the presynaptic neuron. Once inside the neuron, amphetamines force catecholamines out of their storage vesicles and into the synapse. By preventing the reuptake of catecholamines, amphetamines compete for the enzyme monoamine oxidase which is involved in removing dopamine, norepinephrine, and epinephrine (Rosenzweig, 2005). This helps to inhibit the function of the monoamine oxidase
enzyme. And further increases the presence and concentration of these neurotransmitters in the brain for an extended period of time.

**Amphetamine side effects**

There has been substantial controversy over whether or not youth exposure to amphetamines affects their risk for substance abuse. Evidence from recent research has shown that medication does not affect the risk for substance abuse in adolescence (Molina et al., 2013). Amphetamines have also been thought to be harmful to the growth and height of children. This is based on the fact that amphetamines are given during the growth period of childhood and that they cause a loss of appetite which would result in poor health and improper development. This assertion is negated by results from a longitudinal study have demonstrated that there is no correlation of duration of amphetamine treatment and change in height. Therefore amphetamine treatment cannot be attributed to adult height and childhood growth (Harstad et al., 2014).

The most common and prevalent side effects are “suppression, insomnia, irritability, proneness to crying, anxiousness, and nightmares” (Craig et al., 2015). But in the same studies that found these side effects to be the most common ones, also found that most of the participants in the study were able to tolerate the stimulants well. Very few, only 1.6%, had to cease medication treatment because of severe adverse side effects (Efron et al., 1997; Charach et al., 2004). Despite these adverse effects amphetamines do show evidence of improving patient’s symptoms in the short term.
Present Study

The investigation of the effect of amphetamine treatment on executive function and emotional regulation, and if it mitigates the predicted poor life outcomes of children with ADHD

In this study child participants will screened, and then randomly assigned to either a placebo control group or a medication treatment group. Participants in the medication treatment group will receive an individual adjusted dosage long acting mixed amphetamine salts (Adderall), and the placebo control group will receive a sugar pill. Both groups will be observed by their parents. Parents will fill out rating scales based on their child’s executive functioning, emotional regulation, and attentional skills. These measures will be taken at baseline (before treatment), one year into treatment, two years into treatment, and then three years post treatment.

This study has two hypotheses. The first hypothesis will address time and treatment group. In the first hypothesis, it will be predicted that the Adderall treatment group will show a greater improvement overtime than the control group. This will be revealed by a time by treatment interaction. The second hypothesis will address the enduring effects of Adderall treatment overtime. In the second hypothesis it is predicted that there will be a decrement in performance between the two year and five year measure in the Adderall treatment group. This means at the five year measure the control group and the Adderall group will be at the same level of functioning.

Procedure

This study will be a longitudinal multisite double blind placebo controlled study. This design is based off data that this is the most effective form of experimental design for clinical
efficacy studies (Misra, 2012). This study will last for the duration of five years. This will be a multisite study which means it will take place in multiple geographic areas. The raters in this study, who in this case will be the parents of the participants, will be blind to the treatment group that their child will be randomized to. The placebo group will have the same exact characteristics, including the diagnosis of ADHD combined type, as the treatment group. Meaning that all participants will be as uniform as possible in their traits in order to produce the most informed results on the long term efficacy of amphetamine treatment. Eligible participants will be screened for inclusion and exclusion criteria. Inclusion criteria will consist of: (1) the participant must meet at least six symptoms of the DSM-5 criteria for ADHD, combined type, at a moderate to severe level. (2) The participant has a parent and a teacher that will be able to observe them, and fill out routine rating scales. (3) the child is age of eight years at the beginning of the study, male, Caucasian, and from middle to lower socio economic status. Exclusion criteria will consist of: (1) The child has been exposed to a stimulant treatment previous to the current study. (2) The child has been exposed to another intensive intervention or treatment for ADHD, previous to the current study. (3) The child as another comorbid disorder, that significantly impairs their emotional regulation, executive functioning, and or attentional abilities. (4) The child does not give assent to the administration of the treatment (one daily dose of long acting mixed amphetamine, or placebo). (5) Child is not developing normally, in height or weight.
Recruitment

Participants will be recruited through advertisement postings on the Facebook pages of the local chapters of the nonprofit organization Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD) in New York State. There are three local CHADD chapters with individual Facebook pages for parents. Each of these pages has approximately five hundred followers. By sending out these advertisements, it is estimated that the advertisements will reach five hundred participants out of approximately 1,500 Facebook followers. Advertisements (Appendix: A) will be posted to the following Facebook pages:

https://www.facebook.com/CHADD.NewYorkCity

https://www.facebook.com/CHADD-of-Nassau-County-113515095369664/

https://www.facebook.com/CHADDSuffolkCounty
Figure 2. Recruitment procedure for participants. After exclusion criteria, and accounting for loss due to follow up there will be 40 participants, 20 in each treatment group.
Screening Day

After the recruitment period, the eligible participants will undergo a screening day before the study will begin. The screening day will consist of many different procedures to prepare participants for the study. First, all participants and their parents will have a written and oral presentation of a consent form that outlines the study and explains the risks and benefits of their participation (Appendix: B). Parents will also be offered a fifty dollar compensation at each time of measurement for their participation in the study. After consent has been given, children will undergo an independent (to make sure their previous diagnosis still applies) diagnosis of ADHD combined type, with severe to moderate symptoms according to the DSM-5 criteria (Appendix: C), conducted by an onsite child psychiatrist. If they do not meet this criteria they will be excluded from the study. All children will take the Wechsler Intelligence Scale for Children, Third Edition (WISC-III; Wechsler, 1991) (Appendix: D). This test will be conducted by the same child psychiatrist that confirmed their ADHD combined type diagnosis. This test is conducted in order to ensure that children are capable of developmentally appropriate IQ scores, to ensure all children are at the similar level of intelligence and no other contributing factors will confound the present study. The dependent measure of this test is the Full Scale IQ (FSIQ) score, which is the standard score of the child. Scores between 120-129 are classed as "very high", scores between 110-119 are "bright normal", 90-109, average; 85-89, below average; 70-84. If a child scores anything lower than “average” they will be excluded from the study.

A parent rater will be confirmed for each participant. This is in order to ensure that there will be consistent rating scale data throughout the study.
will be given the materials needed for the rating scales. They will be asked and to think about the questions on the rating scales and their child’s general behavior, and to be prepared to fill out the rating scales at their next visit. A week will pass between the screening day and the baseline measure.

**Baseline Measure**

Parents will return to their study site, (which will be their local CHADD chapter), one week after the screening day and complete the rating scales on their child’s behavior. During the parent rating period, children will be randomized into either the placebo or the control group. For the treatment group, they will each receive an individual adjusted dosage of long acting mixed amphetamine salts, and will be called the mixed amphetamine medication (MAM) group. All participants will undergo this evaluation of medication dosage, regardless of treatment group, in order to ensure the blind nature of the study. Only the child psychiatrist will know which treatment group each child is in and will either give the long acting mixed amphetamine, or the placebo pill prescription. After parents have filled out the rating scales and children have been randomized and gone through the clinical consultation, will the baseline measure will be over.

**Procedure of Repeated Measures**

Considering that there is a large amount of time between each measurement day and half of the participants will be medicated with an, amphetamine, it is important to have all children meet with a psychiatrist every six months after treatment has begun, in order to ensure their safety, adjustment to medication dosage, and adverse effects of medication. These checkups will take place at the local CHADD meeting spots and will consist of a consultation with a
psychiatrist and pediatrician. All children regardless of treatment group will come to these checkups because parents will be blind to their treatment group. Only the child psychiatrist will be aware of the child’s treatment group for ethical and safety purposes.

Parents will be given two separate rating scales measuring inhibition, shifting, emotional control, and attention. Parents will be debriefed about how to use each rating scale, and to be particularly observant of their child. Parents will be given sections of the Behavior Rating Inventory of Executive functions, referred to as the BRIEF rating scale (Appendix: E), which is an observational measure of executive functions (Mahone et al., 2002). Parents will also be given the Attention Problems scale (Shapiro, 1999) (Appendix: F). Each of these different rating scales consist of a series of questions about a child’s behavior, intended to capture the level of functioning of emotional control, shifting, inhibition, and attention each child exhibits. Each time of measurement parents will be asked to fill out each of these ratings scales for their children. Measurements will occur before the study begins, which will be a baseline measure of performance, then one year after randomization occurs and amphetamine drug administration begins, there will be a second measure of parent’s ratings on the BRIEF and Attention Problems scale. There will be a third measure two years after the commencement of treatment. After this third measure treatment will be terminated for both groups of children. There will be a three year period between the cessation of treatment and the final measure will be taken three years after treatment. This final measure will consist of the same rating scales that were given to parents throughout the entire study. Parents will be asked to adjust for age on each of the measurement times in order to help control the improvements based on maturation.
The skills of inhibition, shifting, and emotional control will be operationalized through the BRIEF rating scale. Inhibition will be measured through parent ratings on the BRIEF. On the inhibition section of the rating scale, with statements such as “acts wilder or sillier than others in groups (birthday parties, recess)”, with answers of often, sometimes, or never. On the ability for their children to “shift” attention, will be measured with statements such as: “resists or has trouble accepting a different way to solve a problem with schoolwork, friends, chores, etc.” with rating options as often, sometimes, or never. Emotional Regulation will be measured by parent ratings from the BRIEF with statements like “Overreacts to small problems” with ratings of often, sometimes, or never. It is not necessary to have a laboratory measures for the aspects of executive functioning, since it is thought that executive functioning is measured more accurately in real world examples rather than performance on lab tasks. Real world patterns and behaviors of children will be more easy to apply to their lifelong outcomes compared to their reaction time in a laboratory measure.

Attention will be measure through the Attentional Problems rating scale (Shapiro, 1999 & Mahone et al., 2002), with statements like “inattentive, easily distracted”, with rater options of “not true”, “somewhat or sometimes true”, and “often very true” on a 0-2 scale.
Figure 3. Study timeline. There will be a total of four repeated measures, throughout the span of five years. Treatment will be ceased at the end of year two.
Predicted Results

The data and results presented below are based off of previous studies that have investigated the long term effects of amphetamine treatment on children with ADHD (Mcgough et al., 2005). This study combines the design of a longitudinal amphetamine study with the variables of executive functioning and emotional regulation measured by observational rating scales of ADHD symptoms. No study has investigated the long term effects of amphetamine treatment on deficits of executive functioning and emotional regulation caused by inattention in children with ADHD. These specific and targeted impairments are perfect variables, because they are predictors the long term functioning (Mahone, et al., 2002 & Mischel, 1989).

Data Analysis

No significant differences at a p<.05 level are expected to be found in the Attentional Problems Rating scale and the BRIEF rating scale between the two different treatment groups at the baseline measure. This will be confirmed at the baseline measure. During the screening day each group should meet the inclusion criteria of age, race, gender, and socio economic background. Any individual differences will be controlled for by random assignment to each group. Random assignment ensures that differences between the treatment groups will be due to the type of treatment they receive and no other confounding independent variables. It might also be necessary to run a t-test for these demographic variables to verify there will be no significant differences in each of these variables.
Main analyses

To test whether or not MAM treatment will have a significant effect on participant’s executive functioning, emotional control, and attention a 2(treatment: yes/no) X 2(time: baseline/year 1) mixed design (between/within) ANOVA will be conducted in order to determine the effects of the amphetamine treatment and time. Based on previous studies (Mcough et al., 2005), there will be a two way interaction over time. This interaction will be between the two different treatment groups, MAM treatment vs placebo control and time point of baseline and year 1. This significant interaction will demonstrate the efficacy of the amphetamine treatment compared to placebo, during the administration of treatment. There will be an overall main effect of MAM treatment group from baseline measure to the year 1 measure. The MAM group will have a larger reduction in symptoms than the placebo control group. Previous research has already alluded to this finding, but in order to investigate the long term efficacy of the treatment, the level of improvement must be established in the duration of treatment (Mcgough et al., 2005).

Another 2(treatment: yes/no) X 2(time: year 1/year 2) ANOVA will be conducted in order to determine if the amphetamine treatment reduced symptoms, significantly p<.001 from, year 1 to year 2, or if the MAM treatment had a ceiling effect. It is predicted that there will not be a significant effect of the MAM treatment from year 1 to year 2, the medication did have a cut off to the effect it reduced symptoms. The predicted improvements shown on the figure 4, from year 1 to year 2 are due to maturation. The symptom reduction from baseline to year 2 is significant p<.001, and shows a two way interaction of MAM treatment and time point. These results show that the amphetamine treatment is efficacious during long term administration of medication. The
improvements are maintained throughout the duration of administration.

**Figure 4. The reduction of symptoms mediated by treatment group.** The scores of the MAM group on the BRIEF and Attention Problems Rating scale were decreased significantly (lower scores indicate less frequency of behavioral symptoms), in contrast the scores of the placebo control group did not decrease significantly, the only reduction in symptoms shown on the figure was accounted for due to maturation, from baseline to year 1 measurement. The error bars display the standard deviation of error.

A third 2 (treatment: yes/no) × 2 (time: year 2/year 5) ANOVA will be conducted to see whether or not the long term amphetamine treatment had enduring and sustainable effects on the symptoms of ADHD which manifest themselves in impairments in executive functioning, emotional regulation, and attention. This was done by measuring the symptoms of the participants through the Attentional Problems rating scale and BRIEF rating scale for a fourth and final time in each treatment group three years after treatment was concluded. Since there will be significant symptom reduction in the duration of long term treatment, it would be assumed that these effects could be sustained in the participant's function after the cessation of treatment. It is predicted that the MAM group's reduction in symptoms from year 2 to year 5 will not be
sustained.

![Graph showing participant symptoms over time](image)

**Figure 5. The enduring effects of treatment and time.** The scores of the MAM group on the BRIEF and Attentional Problems Scale increased up to levels that mirrored the control group's scores. While the control group's scores decreased a significant amount due to maturation. But both groups ended up with the same deficits in functions, and frequency of poor behavioral symptoms. The error bars display the standard deviation of error.

The progression of each treatment group does improve in the reduction of symptoms. This is improvement in both groups is attributed to maturation considering that the study is conducted over five years from the age of eight to thirteen. These are essential years in development, and the refinement of executive functions, emotional regulation, as well as attentional skills. The reduction of symptoms in the MAM group from baseline to year 1 are significant and are maintained until treatment is ceased at the end of year two. The symptoms steadily rise while the MAM group is no longer on the amphetamine drug, until year 5 where
their symptoms match those in the control group who were never given any form of treatment. Meaning that the amphetamine treatment cannot be determined as efficacious in the long term, if its short term effects cannot be normalized and sustained in an individual’s daily functioning.

**Figure 6. Long term functioning not mediated by MAM treatment.** Initial reduction of symptoms regress to normal level of ADHD functioning. Symptoms decrease through the duration of amphetamine treatment, but return to symptoms similar to the control group after cessation of treatment.
Discussion

This proposed study will test the effects of long term amphetamine treatment. The enduring reduction of impairments in executive functioning, emotional control, and inattention is necessary to establish long term efficacy. The MAM treatment group did show significant improvement in the reduction of symptoms unlike the control group from the baseline measure to the year one measure. The first hypothesis is supported based on the symptom reduction of the MAM group, from obvious positive effects of the treatment. The symptom reduction of the MAM group did not grow, but was maintained from year one measure to the year two measure. This means that amphetamine treatment is efficacious in the short term and is efficacious as long as it is continually administered, but has a ceiling effect.

MAM group lost all effects of symptom reduction from the year 2 measurement to year 5 measurement. Given that amphetamines are only significantly efficacious when consumed, this is problematic because many people diagnosed with ADHD at a young age, stop taking medication around the same time as puberty. This leaves them without coping mechanisms for the detrimental symptoms of ADHD in their daily lives. The improvements from MAM treatment regressed with time. Instead these improvements did not endure in three year time period without medication. Given this evidence, it can be inferred that amphetamine treatment will not mitigate any of the poor life outcomes predicted for those who are diagnosed with ADHD. Another important finding from this study is that the reduction of symptoms on the BRIEF rating scale were correlated with the reduction of symptoms on the Attentional problems rating scale. This finding backs up the theories that attention is the symptom of ADHD that contributes to the impairments in executive functioning and emotional control in people with ADHD.
The real world implications of this study are applicable to the way in which medication perceived as a viable treatment option for children with ADHD. This study demonstrates the need for a change in consciousness of medications like Adderall as a form of treatment for children with ADHD. Research needs to dedicate itself to other methods of treatment for children with ADHD, other than medications. Medications are not a sustainable form of treatment in the long term. The ADHD community needs to understand that medication is not an answer to the disorder but rather an intermediate compensation for improvement behavior and performance. Medication needs to be seen as secondary to developing coping mechanisms that children can normalize into their daily functioning. The image of stimulant treatment needs to be changed from a solution to a short term form of treatment which only helps with day to day functioning. Research should focus on developing alternative intervention programs and therapies that are efficacious in the long term and can be independent of medication.

These proposed significant findings are relevant and important to the development of long term treatments for ADHD. This study is different from other previous studies examining the long term effects of stimulant treatment because it evaluates the improvements from stimulant medication post treatment period. Previous MTA studies have evaluated participant’s performance two, six, and eight years post treatment, but not three years post long term treatment.

Many studies use measurement tools such as performance tasks in order to measure executive functions, emotional control, and attention. This study operationalizes the deficits of these functions through rating scales, which are more applicable to real world impairments of ADHD. The rating scales are also an important measure because unlike performance tasks they
can account for maturation since the rater can adjust their scoring based on age of participant. Amphetamines, like Adderall, are one the most commonly used forms of treatment in children with ADHD. But they can have adverse side effects and do not seem to be able to transform the daily symptom reduction to a reduction in lifelong impairments.

In the interest of the overall goal of this study, it can be inferred that the poor life outcomes will not change with medication. If the MAM treatment group’s improvements have diminished three years post treatment, it can be assumed that they will have the same predicted poor life outcomes as the ADHD children who underwent the placebo treatment. The purpose of this study is to contribute to the body of literature that confirms the inability for amphetamine treatment to be efficacious in the long term reduction of symptoms, so that it may mitigate predicted poor life outcomes for those who ADHD.

**Limitations**

This study is based off many previous studies. This study combines research of long term amphetamine efficacy, and the deficits in executive functions and emotional regulation in children with ADHD. This study has limitations that could have acted as confounds in the study design, and affected the overall results. A longitudinal study design always comes with confounds. It is possible, that throughout the five years the DSM-5 diagnosis of ADHD combined type with moderate to severe symptoms stopped applying to some of the participants in either the placebo or treatment group. This would make their performance on the rating scales no longer pertinent to the study. Maturation could have affected the participants performance on the rating scales. Their performance on the rating scales could also be different due to changes in their behavior because inattention manifests itself inwardly instead of outwardly with age in
ADHD. Another confound is that when parents are raters of their own children they can contribute to reporting bias. It could also be inaccurate reporting because children’s behavior could be different in a home setting rather than in a social or school setting. Children may have also acted differently knowing that they were receiving a type of medication even if it was the placebo, demonstrating a placebo effect. Children may have had undetected learning disabilities or comorbid disorders that contributed to their deficits in executive functioning emotional regulation. Compensation could have altered a family’s participation and performance in the study. For example not filling out the rating scales accurately.

Having a placebo control group always has ethical implications. A placebo control group can be seen as denying treatment to some participants who have the disorder. Future studies might want to use a normative comparison group, which in this case would be children with the same traits as the MAM group, except for the diagnosis of ADHD. This way the longitudinal study would test if the MAM group was functioning at the same or close to the same level as the normative comparison group. If the treatment was efficacious in the long term, the MAM group would be functioning at the same level as the normative comparison group. Ethical concerns are always present when working with child participants. Making sure that children are giving full assent throughout the entire duration of the study is difficult to ensure fully. This needs to be communicated fully and extensively to guardians or parents to make sure the child is not unwillingly undergoing treatment.

In the future it could be beneficial to run a similar study, but have more measures that occur after the cessation of treatment for each different group. This would be to determine at which exact point after the cessation of treatment do ADHD symptoms start to return for the
MAM treatment group.

Future studies should focus on confirming this long term flaw in amphetamine treatment. In order to publish enough literature and data to spread the message of an unsustainable treatment to the ADHD community. This could potentially help decrease the unnecessary distribution of amphetamines and further reduce its abuses amongst the non ADHD population. The most important population to reach would be pediatricians and psychiatrists who are the ones that prescribe these medications. Pediatricians and psychiatrists need to fully communicate to parents the new research indicating that amphetamines are not efficacious in the long term. Therefore, amphetamines will not end up improving their child’s long term functioning at home or at school. This might encourage parents to seek alternative methods in order to help their child develop appropriate coping skills that they can keep for the entirety of their lives.
Conclusion

From these results, it can be inferred that the efficacy of amphetamine treatment is specific to administration. This means that this treatment is efficacious but has no lasting effects which invalidates its true efficacy. Executive functioning and emotional regulation were good variables to measure this efficacy because they are obvious behavioral symptoms of ADHD and are predictors of life outcomes. If amphetamine treatment could have sustained long term improvements in the impairments of executive functioning and emotional regulation in children with ADHD. This would mean that it would be an efficacious treatment method in the long term. Therefore, it would mitigate predicted poor life outcomes for those diagnosed with ADHD.

This study contributes to a greater body of literature, which established that amphetamine treatments are not efficacious in the long term. Medication treatment cannot improve the predicted poor life outcomes of ADHD. This is because medication cannot sustain a reduction in the impairments of executive functioning and emotional regulation, which seem to be contributors to the predicted poor life outcomes. This evidence should be used to encourage an increase in behavioral therapies. Since the largest population of children affected by ADHD are from lower socio economic background and their families often do not have the resources and time to allot to behavioral therapy, other alternative therapies should be developed, like a school exercise programs, or school enforced extra play time for children with ADHD (Cordier et al., 2009; Katz et al., 2010; Grassmann et al., 2014). There needs to be a renewed focus on behavioral therapies, and other alternative therapies that will be more efficacious in the long term symptom reduction of ADHD.
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LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD


LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD


LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

doi:10.3928/15394492-20090501-01


Long Term Efficacy of Stimulant Treatment in ADHD


LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

444-454. doi:10.1037/adb0000039


LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

doi:10.1080/10673220802167782


Mcgough, J. J., Biederman, J., Wigal, S. B., Lopez, F. A., Mccracken, J. T., Spencer, T., & ...

doi:10.1097/01.chi.0000157550.94702.a2


Marcus, S. (2013). Adolescent Substance Use in the Multimodal Treatment Study of Attention-Deficit/Hyperactivity Disorder (ADHD) (MTA) as a Function of Childhood


http://doi.org/10.1371/journal.pone.0128248


http://dx.doi.org/10.1097/00004583-199706000-00011


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Appendix A: Facebook Advertisement

Does your child have ADHD?

Have you not found the right treatment for your child?

Come participate in a study that could give your child the treatment you have been looking for!!!

Come participate in a study that could benefit children all around the world with ADHD!

Please contact Kaitlyn Mock at katiemock@gmail.com if you think this study could apply to you and your child!
Appendix B: Consent Form

The Purpose of this study:
This study is being conducted in order to investigate the long term efficacy of amphetamine treatment in children with ADHD.

This study includes:
Child participants with a clinical diagnosis of ADHD. They will be randomized to either receive a dosage of mixed amphetamine salts, Adderall, or a placebo treatment. All participants will require a parent to give feedback on rating scales three times in three years. Throughout these three years participants will have clinical check-up every six months, in order to adjust and keep track of medication dosage. Participants and their parents will then be contact three years after treatment for one additional feedback on the rating scales.

Risks and benefits of this study:
Amphetamines have been shown to produce adverse side effects, but participants will have routine checkups, and any participants who are having adverse effects will discontinue participation in the study, and will still receive compensation. Participants and their parents will have to commit to time commitments throughout the two years of treatment. Benefits include the chance of amphetamine treatment for children with ADHD have a positive effect on ADHD symptoms in the duration of treatment.

Statement of confidentiality:
All information that participants and their families submit to this study will be completely confidential. The identities of participants and their families will be confidential.

Compensation:
For each time of measurement, meaning each time parent rating scales are turned in, parents will receive a 50$ stipend for their time and resources.

Contact information:
Kaitlyn Mock:
(828)481-2673
Katienmock@gmail.com

Statement of consent:
By signing below you are indicating that you are giving informed to consent for you and your child to participant in this study. Please talk to your child about this study, and make sure the child gives assent for their participation in the study.

Assent:
Since this study involves child participants who will be ingesting an amphetamine. It is imperative for parents to ensure their child is willing and capable of giving proper assent to this
study before participation. The child should express approval and agreement to the study once it has been described to them and what will be required of them.

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been given an opportunity to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have additional questions. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time."

Sign Here: ____________________________________
LONG TERM EFFICACY OF STIMULANT TREATMENT IN ADHD

Appendix C: DSM-5 Diagnostic Criteria

Overview of the DSM-5™ medical classification system for ADHD

- A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development
  - Six or more of the symptoms have persisted for at least six months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities. Please note: The symptoms are not solely a manifestation of oppositional behaviour, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), five or more symptoms are required
  - Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years
  - Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g. at home, school, or work; with friends or relatives; in other activities)
  - There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic or occupational functioning
  - The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g. mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal)

Presentations of ADHD

Individuals with ADHD may present with both inattention and hyperactivity/impulsivity, or one symptom pattern may predominate. Three presentations of ADHD are commonly referred to: combined-type, inattentive-type and hyperactive/impulsive-type (Table 1). According to the DSM-5™ classification system, the appropriate presentation of ADHD should be indicated based on the predominant symptom pattern for the last six months.¹

Table 1: Presentations of ADHD¹

<table>
<thead>
<tr>
<th>Presentations of ADHD¹</th>
<th>Combined</th>
<th>Inattentive</th>
<th>Hyperactive/Impulsive</th>
</tr>
</thead>
<tbody>
<tr>
<td>All three core features are present and ADHD is diagnosed when ≥6 symptoms of hyperactivity/impulsivity and ≥6 symptoms of inattention have been observed for ≥6 months</td>
<td>Diagnosed if ≥6 symptoms of inattention (but &lt;6 symptoms of hyperactivity/impulsivity) have persisted for ≥6 months</td>
<td>Diagnosed if ≥6 symptoms of hyperactivity/impulsivity (but &lt;6 symptoms of inattention) have been present for ≥6 months</td>
<td></td>
</tr>
</tbody>
</table>

Furthermore, the DSM-5™ also states that it must be specified whether the individual with ADHD is in “partial remission” (when partial ADHD criteria have been met for the past six months with full criteria met previously, and the symptoms still result in impairment in social, academic or occupational functioning); and the current severity of the disease (Table 2).¹

Table 2: Current severity of ADHD¹

<table>
<thead>
<tr>
<th>Current severity of ADHD¹</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning</td>
<td>Symptoms or functional impairment between “mild” and “severe” are present</td>
<td>Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present; or the symptoms result in marked impairment in social or occupational functioning</td>
<td></td>
</tr>
</tbody>
</table>
Appendix D: Sample Intelligence Test Scoring Table
Appendix E: BRIEF Rating Scale

**Inhibit**

The Inhibit scale assesses inhibitory control and impulsivity. This can be described as the ability to resist impulses and the ability to stop one’s own behavior at the appropriate time. Sample’s score on this scale is clinically elevated ($T = 72, \text{ %ile } = 96$) as compared to his peers. Children with similar scores on the Inhibit scale typically have marked difficulty resisting impulses and difficulty considering consequences before acting. They are often perceived as (1) being less in control of themselves than their peers, (2) having difficulty staying in line or in the classroom, (3) interrupting others or calling out in class frequently, and (4) requiring higher levels of adult supervision. Often, caregivers and teachers are particularly concerned about the verbal and social intrusiveness and the lack of personal safety observed in children who do not inhibit impulses well. Such children may display high levels of physical activity, inappropriate physical responses to others, a tendency to interrupt and disrupt group activities, and a general failure to look before leaping.

In the contexts of the classroom and assessment settings, children with inhibitory control difficulties often require a higher degree of external structure to limit their impulsive responding. They may start an activity or task before listening to instructions, before developing a plan, or before grasping the organization or gist of the situation.

Examination of the individual items that comprise the Inhibit scale may be informative and may help guide interpretation and intervention.
<table>
<thead>
<tr>
<th>Item #</th>
<th>Inhibit items</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>is fidgety</td>
<td>Often</td>
</tr>
<tr>
<td>10</td>
<td>Remaining content redacted for sample report purposes</td>
<td>Often</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>Sometimes</td>
</tr>
<tr>
<td>39</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>48</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>62</td>
<td></td>
<td>Never</td>
</tr>
</tbody>
</table>
Emotional Control

The Emotional Control scale measures the impact of executive function problems on emotional expression and assesses a child’s ability to modulate or regulate his or her emotional responses. Sample’s score on the Emotional Control scale is clinically elevated compared with peers ($T = 73$, %ile = 96). This score suggests marked concerns with regulation or modulation of emotions. Sample likely overreacts to events and likely demonstrates sudden outbursts, sudden and/or frequent mood changes, and excessive periods of emotional upset. Poor emotional control is often expressed as emotional lability, sudden outbursts, or emotional explosiveness. Children with difficulties in this domain often have overblown emotional reactions to seemingly minor events. Caregivers and teachers of such children frequently describe a child who cries easily or laughs hysterically with small provocation or a child who has temper tantrums of a frequency or severity that is not age appropriate.

<table>
<thead>
<tr>
<th>Item #</th>
<th>Emotional Control items</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Has explosive, angry outbursts</td>
<td>Often</td>
</tr>
<tr>
<td>14</td>
<td>Remaining content redacted for sample report purposes</td>
<td>Sometimes</td>
</tr>
<tr>
<td>22</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>27</td>
<td></td>
<td>Sometimes</td>
</tr>
<tr>
<td>34</td>
<td></td>
<td>Sometimes</td>
</tr>
<tr>
<td>43</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>51</td>
<td></td>
<td>Sometimes</td>
</tr>
<tr>
<td>56</td>
<td></td>
<td>Often</td>
</tr>
</tbody>
</table>
The Shift scale assesses the ability to move freely from one situation, activity, or aspect of a problem to another as the circumstances demand. Key aspects of shifting include the ability to make transitions, tolerate change, problem solve flexibly, switch or alternate attention between tasks, and change focus from one task or topic to another. Mild deficits may compromise efficiency of problem solving and result in a tendency to get stuck or focused on a topic or problem, whereas more severe difficulties can be reflected in perseverative behaviors and marked resistance to change. Sample’s score on the Shift scale is within the average range compared with peers ($T = 56$, %ile = 77). This suggests that Sample is generally able to change from task to task or from place to place without difficulty, is able to think of or accept different ways of solving problems, and is able to demonstrate flexibility in day-to-day activities.

<table>
<thead>
<tr>
<th>Item #</th>
<th>Shift items</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Resists or has trouble accepting a different way to solve a problem with schoolwork, friends, tasks, etc.</td>
<td>Never</td>
</tr>
<tr>
<td>11</td>
<td><strong>Remaining content redacted for sample report purposes</strong></td>
<td>Never</td>
</tr>
<tr>
<td>17</td>
<td></td>
<td>Sometimes</td>
</tr>
<tr>
<td>31</td>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>40</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>49</td>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>58</td>
<td></td>
<td>Often</td>
</tr>
<tr>
<td>60</td>
<td></td>
<td>Never</td>
</tr>
</tbody>
</table>
## BRIEF®2 Parent Score Summary Table

<table>
<thead>
<tr>
<th>Index/scale</th>
<th>Raw score</th>
<th>T score</th>
<th>Percentile</th>
<th>90% C.L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit</td>
<td>21</td>
<td>72</td>
<td>96</td>
<td>66-78</td>
</tr>
<tr>
<td>Self-Monitor</td>
<td>10</td>
<td>68</td>
<td>97</td>
<td>61-75</td>
</tr>
<tr>
<td>Behavior Regulation Index (BRI)</td>
<td>31</td>
<td>72</td>
<td>97</td>
<td>67-77</td>
</tr>
<tr>
<td>Shift</td>
<td>13</td>
<td>56</td>
<td>77</td>
<td>49-63</td>
</tr>
<tr>
<td>Emotional Control</td>
<td>20</td>
<td>73</td>
<td>96</td>
<td>68-78</td>
</tr>
<tr>
<td>Emotion Regulation Index (ERI)</td>
<td>33</td>
<td>66</td>
<td>93</td>
<td>61-71</td>
</tr>
<tr>
<td>Initiate</td>
<td>14</td>
<td>75</td>
<td>≥ 99</td>
<td>68-82</td>
</tr>
<tr>
<td>Working Memory</td>
<td>21</td>
<td>72</td>
<td>97</td>
<td>67-77</td>
</tr>
<tr>
<td>Plan/Organize</td>
<td>24</td>
<td>79</td>
<td>≥ 99</td>
<td>73-85</td>
</tr>
<tr>
<td>Task-Monitor</td>
<td>14</td>
<td>69</td>
<td>97</td>
<td>62-76</td>
</tr>
<tr>
<td>Organization of Materials</td>
<td>16</td>
<td>70</td>
<td>97</td>
<td>64-76</td>
</tr>
<tr>
<td>Cognitive Regulation Index (CRI)</td>
<td>89</td>
<td>75</td>
<td>≥ 99</td>
<td>72-78</td>
</tr>
<tr>
<td>Global Executive Composite (GEC)</td>
<td>153</td>
<td>78</td>
<td>≥ 99</td>
<td>76-80</td>
</tr>
</tbody>
</table>

### Validity scale

<table>
<thead>
<tr>
<th>Raw score</th>
<th>Percentile</th>
<th>Protocol classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negativity</td>
<td>2</td>
<td>≤ 98</td>
</tr>
<tr>
<td>Inconsistency</td>
<td>4</td>
<td>≤ 98</td>
</tr>
<tr>
<td>Infrequency</td>
<td>0</td>
<td>99</td>
</tr>
</tbody>
</table>

Note: Male, age-specific norms have been used to generate this profile.

For additional normative information, refer to Appendices A–C in the BRIEF®2 Professional Manual.
Appendix F: Attentional Problems Rating Scale

Clinical Attention Problem Scale
Please complete once a week

Child's name: _______________________________  Today's date: ________________
Completed by: _______________________________  Medication: ____________________

Below is a list of items that describe pupils. Rate each item that describes the pupil now or within the last week as follows:
0 = Not true  1 = Somewhat or Sometimes True  2 = Very or Often True

<table>
<thead>
<tr>
<th>Morning</th>
<th>Afternoon</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fails to finish things he/she starts</td>
<td>1. Fails to finish things he/she starts</td>
</tr>
<tr>
<td>2. Can't concentrate, can't pay attention for</td>
<td>2. Can't concentrate, can't pay attention for</td>
</tr>
<tr>
<td>long</td>
<td>long</td>
</tr>
<tr>
<td>3. Can't sit still, restless, or hyperactive</td>
<td>3. Can't sit still, restless, or hyperactive</td>
</tr>
<tr>
<td>4. Fidgets</td>
<td>4. Fidgets</td>
</tr>
<tr>
<td>5. Daydreams or gets lost in his/her thoughts</td>
<td>5. Daydreams or gets lost in his/her thoughts</td>
</tr>
<tr>
<td>6. Impulsive, or acts without thinking</td>
<td>6. Impulsive, or acts without thinking</td>
</tr>
<tr>
<td>7. Difficulty following directions</td>
<td>7. Difficulty following directions</td>
</tr>
<tr>
<td>8. Talks out of turn</td>
<td>8. Talks out of turn</td>
</tr>
<tr>
<td>10. Inattentive, easily distracted</td>
<td>10. Inattentive, easily distracted</td>
</tr>
<tr>
<td>11. Talks too much</td>
<td>11. Talks too much</td>
</tr>
<tr>
<td>12. Fails to carry out assigned tasks</td>
<td>12. Fails to carry out assigned tasks</td>
</tr>
</tbody>
</table>

Additional Comments: _______________________________

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Additional copies are available on the Pediatric Development and Behavior Homepage, http://www.dbpeds.org/handouts/
Appendix G: IRB Proposal

Title:
The long term efficacy of stimulant treatment in executive functioning and emotional regulation in attention-deficit/hyperactivity disorder

Research Question:
ADHD is a persistent pervasive disorder that usually lasts throughout the lifespan for those diagnosed in childhood. Children who are diagnosed with ADHD, often have predicted poor life outcomes compared to those without ADHD. Numerous treatment methods for ADHD have been developed since the discovery of the disorder. Although the CDC and the APA recommend combined treatment of behavioral therapy, stimulant treatment, as well as school interventions, this is not occurs when a diagnosis occurs in childhood. Stimulants have become the first line for treatment due to their immediate and short term effectiveness in reducing symptoms of ADHD. The long term efficaciousness of stimulant treatment in ADHD has not yet been established. Since the long term implications of stimulant treatment in ADHD has not been established, then why is it being used as a first line of treatment for children? Executive functioning and emotional regulation have also been shown to be strong predictors of life outcomes. Deficits in executive functioning and emotional regulation are deficits that are also found in ADHD. These deficits could be contributing factors to the predicted poor life outcomes in children with ADHD. Is stimulant treatment efficacious in improving the deficits in executive functioning and emotional regulation in the long term, in order to mediate the predicted poor life outcomes?

Procedure:
This study will be a multisite double blind placebo controlled study. Eligible participants will be screened for inclusion and exclusion criteria. Inclusion criteria will consist of: (1) the participant must meet at least six symptoms of the DSM-5 criteria for ADHD, combined type, at a moderate to severe level. (2) The participant has a parent and a teacher that will be able to observe them, and fill out routine rating scales. (3) The child is age eight at the beginning of the study, male, Caucasian, and from middle to lower socio economic status. Exclusion criteria will consist of: (1) The child has been exposed to a stimulant treatment previous to the current study. (2) The child has been exposed to another intensive intervention or treatment for ADHD, previous to the current study. (3) The child as another comorbid disorder, that significantly impairs their emotional regulation, executive functioning, and attentional abilities. (4) The child does not give assent to the administration of the treatment (one daily dose of methylphenidate, or placebo). (5) Child is not developing normally, in height or weight.

Recruitment will consist of advertisements posted to the local CHADD Facebook pages of New York state.

After the recruitment period, the eligible participants will undergo a screening day before the study will begin. The screening day will consist of an independent diagnosis of all children with ADHD combined type, with severe to moderate symptoms according to the DSM-5 criteria, conducted by an on site child psychologist. If they do not meet this criteria they will be excluded from the study. All children will take the Wechsler Intelligence Scale for Children, Third Edition (WISC-III; Wechsler, 1991). This test will be conducted by the same child psychologist that
confirmed their ADHD combined type diagnosis. This test is conducted in order to ensure that children are capable of developmentally appropriate IQ scores, to ensure all children are at the similar level of intelligence and no other contributing factors will confound the present study. If a child scores anything lower than “average” they will be excluded from the study. A parent rater will be confirmed for each participant, in order to ensure that their will be consistent rating scale reporting and data throughout the study. At the end of the screening day parents will be given the materials needed for the rating scales, and to think about the questions asked on the rating scales and their child’s general behavior. A week will pass between the screening day and the baseline measure. Parents will return to their study site, (which will be their local CHADD chapter), one week after the screening day and complete the rating scales on their child’s behavior. During the parent rating period children will be randomized into either the placebo or the control group.

Procedure of Repeated Measures:
Parents will each be debriefed about how to use each rating scale, and to be particularly observant of their child or student. Parents will be given sections of the Behavior Rating Inventory of Executive function (BRIEF) rating scale, which include emotional control, inhibit, and shifting. Parents will also be given the Attention Problems scale. Each of these different rating scales consist of a series of questions about a child’s behavior, intended to capture the level of functioning of emotional control, shifting, inhibition, and attention each child exhibits. Each time of measurement parents will be asked to fill out each of these ratings scales for their children. Measurements will occur before the study begins, which will be a baseline measure of performance, then one year after randomization occurs and stimulant or drug administration begins, there will be a second measure of parent’s ratings on the BRIEF and Attention Problems scale. There will be a third measure two years after the commencement of treatment. After this third measure treatment will be terminated for both groups of children. There will be a three year period between the cessation of treatment and the final measure. This final measure will consist of the same rating scales that were given to parents throughout the entire study. Parents will be asked to adjust for age on each of the measurement times in order to help control the improvements based on maturation.

Recruitment of participants:
Participants will be recruited through flyer advertisements, that will be posted at the meeting spots for the local chapters of the nonprofit organization Children and Adults with Attention Deficit Disorder in New York state.

Number of Participants
There will be twenty participants recruited for each treatment group. In total there will be forty participants.

Risks and Benefits:
Due to the nature of stimulant medications, there is always a risk of adverse side effects. Another considered risk would be for parents, to involve their child in the study, who has ADHD, and never receive treatment, because they are randomly placed in the placebo control group.

Compensation:
At each time of measurement parents will be compensated with 50$, upon successful completion of the rating scales.

Consent:
Consent from both parents, and assent from the child will be required for participation in the study.

Hypotheses:
This study has two hypotheses. The first hypothesis will address time and treatment group. In the first hypothesis, it will be predicted that the Adderall group will show a greater improvement overtime than the control group. This will be revealed by a time by treatment interaction. The second hypothesis will address the enduring effects of Adderall treatment overtime. In the second hypothesis it is predicted that there will be a decrement in performance between the two year and five year measure in the Adderall treatment group. This means at the five year measure there would be an interaction between control and Adderall group meaning that they would be at the same level of functioning.
Appendix H: Certification to work with human subjects

Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that Kaitlyn Mock successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 03/28/2017.

Certification Number: 2362882.
Appendix I: Budget Proposal

<table>
<thead>
<tr>
<th>Expense type</th>
<th>Cost per Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adderall medication</td>
<td>6,000$</td>
</tr>
<tr>
<td>ADHD evaluations and diagnosis</td>
<td>5,000$</td>
</tr>
<tr>
<td>Intelligence test</td>
<td>100$</td>
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<tr>
<td>Rating scales</td>
<td>100$</td>
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<tr>
<td>Study administrators</td>
<td>1,000$</td>
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<tr>
<td>Multisite CHADD access</td>
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<tr>
<td>Compensation for parents</td>
<td>200$</td>
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<tr>
<td>Follow-up evaluators and administrators</td>
<td>2,000</td>
</tr>
<tr>
<td>Data accumulation and analysis</td>
<td>5,000</td>
</tr>
</tbody>
</table>

Total cost per participant: 20,000$

Other miscellaneous costs: 200,000$

Total cost of study: 1,000,000$