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Maryam Jeirooti

University of the Pacific, [sjmb82@yahoo.com](mailto:sjmb82@yahoo.com)

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**A comparison of the effect of pharmacological therapy, behavioral therapy, and combination therapy in adults with ADHD**

By

Maryam Jeiroodi

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## **A comparison of the effect of pharmacological therapy, behavioral therapy, and combination therapy in adults with ADHD**

### **Introduction**

Attention Deficit Hyperactivity Disorder (ADHD) is defined as a neurodevelopmental disorder causing inattention, disorganization, and/or hyperactivity-impulsivity.<sup>1</sup> As a consequence of ADHD symptoms, affected children may fall behind their peers in academics and social life. Although the severity of some symptoms may subside as the individual ages, they may persist throughout life.<sup>2</sup>

The Centers for Disease Control and Prevention (CDC)'s 2016 report states that 9.4% of U.S. children, 2-17 years old, have been diagnosed with ADHD. From this group of children, 8.4% have a persistent diagnosis of ADHD that remains into adulthood.<sup>3</sup> ADHD prevalence amongst U.S. adults aged 18-44 years was 8.1% in 2005.<sup>4</sup> A 2019 publication of a cohort study reported an increase of 123.3% in prevalence of new diagnoses of ADHD in adults between January 2007 and December 2016, whereas the prevalence in children increased only by 26.4% during the same period.<sup>5</sup>

Although the Diagnostic and Statistical Manual of Mental Disorders 5<sup>th</sup> edition (DSM-5) holds specific criteria for the diagnosis of ADHD in adults, this was not always the case, and early editions of the DSM considered ADHD a neurodevelopmental disorder only in children. The consensus was that the condition improved with age.<sup>6</sup> Per the DSM-5, hyperactivity symptoms in adulthood may present as restlessness or wearing others out with their activity, but the inattention may remain the same. Since ADHD was exclusively a diagnosis in children, many adults have never been diagnosed, and unaware of their condition, they might have lived under constant negative feedback from parents, teachers and even peers. Long-term consequences of this exposure could be maladaptive behaviors, low self-esteem, depression, anxiety, and deficiencies in education, careers, and relationships.<sup>7</sup>

The standard of care for children recommends psychotherapy as the first line. Additionally, parental and school education have shown to be efficacious. Pharmacotherapy with stimulant medications is considered second line of therapy in children,<sup>6</sup> whereas in adults, pharmacotherapy is the main treatment.<sup>8</sup> Stimulants such as methamphetamines and methylphenidates have shown to be efficacious in controlling the core symptoms of ADHD in adults; however, there are several factors that could make cognitive behavioral therapy an integral part of the management of ADHD in adults. Of the adults with ADHD who are treated with medications, 20-50% may not see sufficient improvement in their core symptoms, or they may not tolerate the medications. Moreover, studies have shown those who respond to medications may only see about a 50% reduction in their core symptoms. Finally, the responders to medications may become stable with medications, but they have not learned the skills required to cope with their daily challenges at school, work, and home. Behavioral therapy has been shown to be effective in filling this gap.<sup>9</sup>

The goal of this review is to compare the efficacy of pharmacological therapy and behavioral therapy to combination therapy in adults who are diagnosed with ADHD. Several studies are reviewed including randomized controlled trials (RCT) and meta-analyses with the goal of comparing behavioral therapy and pharmacotherapy with each other, with control groups, with waiting list groups, and with combination therapy.

## **Discussion**

### **Equivocal effect of therapies on core symptoms of ADHD**

In an RCT study of combination therapy consisting of behavioral therapy and medications, in comparison to behavioral therapy alone, Mei-Rong et al found that there was no superiority in combination therapy in the reduction of the core symptoms of ADHD: inattention, impulsivity, and

hyperactivity. However, the group that received combination therapy demonstrated a significant improvement in executive functions, such as self-monitoring, planning, and organizing, compared to the behavioral therapy group.<sup>10</sup>

The primary outcome of this study was that behavioral therapy, in both monotherapy and combination therapy, resulted in a significant improvement of the ADHD core symptoms. Contrary to hypothesis, the study did not find superior efficacy of combination therapy compared to behavioral therapy alone. Similarly, the secondary outcome showed no significant superiority of combination therapy in the management of anxiety, depression, and self-esteem.<sup>10</sup>

A limitation of this study is that most of the participants were highly educated and had high IQs, which could explain why both groups showed similar results. Additionally, the study did not use a placebo in the behavioral therapy group. Placebos have strong effects on participants, when they believe they are taking medications to treat their ADHD; therefore, the placebo effect in this study cannot be ruled out.<sup>10</sup>

Weiss et al conducted a similar double-blind RCT but included a placebo in the group that only received behavioral therapy. The question was whether the addition of medication to behavioral therapy could change the outcome. The study reported no statistically significant difference between the group that received medication and behavioral therapy and the group that received placebo and behavioral therapy.<sup>11</sup> The behavioral therapy was customized for each patient to meet their shortcomings (i.e., time management, relaxation, productivity at work or school, anger management) and focused on providing skills and home exercises for the patients so that they could learn and maintain their skills and outcomes.

In comparison with the Mei-Rong et al study that had highly educated participants, Weiss's study had participants from five different geographic locations. Although Weiss's study does not provide any information about participants' educational backgrounds, its findings are more generalizable since the individuals presented with a variety of ADHD maladaptation in executive functioning consistent with what is commonly seen in ADHD patients.

On the other hand, this study cannot demonstrate whether behavioral therapy on its own is enough for treating ADHD core symptoms and secondary executive dysfunction because no group received only behavioral therapy. These two studies followed the participants only for five to twelve months after the completion of the therapies, therefore, no data show whether the effect of behavioral therapy was sustained long-term.

In a meta-analysis, Knouse et al tried to observe whether behavioral therapy is the superior treatment modality for adults with ADHD. After analyzing 32 studies, they were not able to show that behavioral therapy is superior to medication therapy. Addition of behavioral therapy for participants who were already taking medications, did not necessarily show larger therapy effects.<sup>12</sup> But lack of a larger therapy effect does not mean it does not exist. They noticed in studies that behavioral therapy was offered to two groups: one was taking medications and the other was not, both groups showed significant improvements, but none was better than the other.<sup>12</sup>

Additionally, the researchers believe that since behavioral therapies come in different forms, patients and providers have different options to choose from. This can help providers to individualize treatment plans for their patients. Moreover, they found some of these therapies had greater effects, such as better outcomes with cognitive-behavioral therapy compared to dialectical behavioral therapy or biofeedback. Therefore, knowing more about the details of the patients'

symptoms and the severity of them can help providers to select the best therapy suitable for addressing specific symptoms.

On the other hand, the researchers determined that most of the studies included in the meta-analysis had interventions that helped the inattention symptom of ADHD and less of the hyperactivity. Therefore, more research is needed to address this aspect of ADHD, too; although, adults usually suffer more from inattention and less from hyperactivity. The hyperactivity-impulsivity symptom can manifest as making important decisions without thinking them through, or impulsively investing money in something that has no profitable return. Thus, the grave outcomes of such behaviors emphasize the importance of managing both the hyperactivity-impulsivity symptoms as well as the inattention symptom.

Finally, the authors emphasize the need for additional studies regarding behavioral therapy of adults with ADHD because there is simply not enough data available to give a robust conclusion. They also suggest that there should be a Gold Standard measuring tool for evaluation of patients in future studies, so that the results are not as heterogeneous and difficult to correlate with each other.

#### **Data in favor of combination therapy**

Safren et al conducted an RCT to study the efficacy of combination therapy in comparison to stabilized medication therapy in adults with ADHD, with the hypothesis that combination therapy is superior. The study indeed showed promising results in the group that received the combination therapy. This group had statistically reliable and clinically significant improvement in their ADHD core symptoms of inattention, impulsivity, and hyperactivity. As the secondary outcome of the

study, this group also showed significantly reduced anxiety and depression scores compared to the group that only received medication therapy.<sup>9</sup>

In this study, all patients received training in organization and planning, coping with distractibility, and cognitive restructuring. They also could choose to receive additional training for one of the following: procrastination, anger management, or communication skills. Following the completion of the assessments, the group that only received medication therapy was offered behavioral therapy, too. Although this group was prohibited from changing their medications over the course of the study, a few of the participants' physicians changed their medications. As a result, the researchers analyzed the replication of the study after excluding these participants from the analysis and found that it had no effect on the results.

#### **Data in favor of behavioral therapy**

A meta-analysis compared studies that used cognitive-behavioral therapy as an intervention with an active control group and with a waitlist group. The active control group received other types of therapy such as relaxation, educational support, and supportive psychotherapy. They found that two-thirds of the studies showed superiority in cognitive-behavioral therapy intervention in controlling ADHD core symptoms, and one-third found a negative trend, meaning other types of therapy showed better results compared to cognitive-behavioral therapy. Analysis of the studies that compared cognitive-behavioral therapy with waitlist groups was also in favor of cognitive-behavioral therapy.<sup>14</sup>

The result of this meta-analysis appears more generalizable because in some of the studies with active control groups, the participants received unrelated therapy that required weekly interactions with therapists, unlike the waitlist participants who received no attention. These

measures can be helpful in keeping the participants blinded because they assume that all participants have received the intervention.<sup>14</sup> Although, some experts believe that such measures belong to pharmacotherapy studies and should not be used in psychotherapy research.<sup>15</sup> In some of the psychotherapy studies, instead of a placebo group, a waitlist group was used with the intention of lowering the likelihood of bias and having a comparison group to measure the effect of the intervention. Depending on the intentions of the individuals who participate in psychotherapy studies, assignment to a waitlist group or intervention group can potentially alter the results of a study.<sup>16</sup> If an individual joins a study for financial gain but is randomly assigned to the intervention group, it is possible to see non-compliance in such an individual. Likewise, if an individual joins a study in hope of receiving help but is randomly assigned to a waitlist group, it is possible to see disappointment and discontinuation of participation depending on how long they have to wait.<sup>16</sup> All such possibilities must be considered in the design of a psychotherapy study to increase the validity and generalizability of findings.

## **Conclusion**

Although none of these studies can be used as guidelines for the treatment of ADHD in adults, the collective knowledge gained from them can shed light on the different aspects of ADHD, and not only its core symptoms. As discussed, individuals suffering from ADHD usually suffer from comorbidities such as anxiety and depression that are a direct result of their ADHD and their lack of coping skills. Therefore, without providing a definite treatment for ADHD, these studies provide tools that can help medical providers design an individualized treatment plan for their adult patients suffering from ADHD, especially those who are first diagnosed in adulthood.

While patients should be provided with treatment options—medication, behavioral therapy or both—the main question remains, and that is what happens in the long term. Therefore, more studies

are needed to shine light on the long-term side effects of stimulant medications and whether behavioral therapy gains last for years to come. There is also no definite treatment option based on the severity of symptoms. Further studies are needed to investigate whether patients with more severe symptoms benefit from increasing the dosage of their medications or the addition of another class of drugs to their regimen, or if they are better off with the addition of behavioral therapy. Additionally, the higher cost of behavioral therapy is a barrier to treatment for many patients. Perhaps insurance coverage for such therapies could help in removing such barriers.

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