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Review

A Review of Efficacy and Neural Mechanisms of Adult ADHD and ASD Treatments

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Abstract: Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are prevalent neurodevelopmental problems for many people, and usually followed them from childhood to adulthood. While many approaches, such as pharmacological, like stimulants; behavioral, like Cognitive Behavioral Therapy; physical interventions, like DCS; are available, their comparative efficacy and underlying neural mechanisms are not clear at all. This review will analyzes current evidence of those treatments and summarizes their neuropsychological basis. By providing a comprehensive overview of existing treatment options, this review aims to help clinical decision-making for medical care workers and guide and search the possibility of related future research for more individualized interventions for adults with ADHD or ASD.

Keywords: Autism Spectrum Disorder; Attention-Deficit/Hyperactivity Disorder; Adult neurodevelopmental disorders; Treatment efficacy; Neural mechanisms; Pharmacological interventions; Behavioral therapy

1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are two major neurodevelopmental disorders that often persist from childhood into adulthood, significantly affecting individuals' daily functioning and quality of life [1]. Individuals with ADHD may experience core symptoms such as attention deficits, emotional dysregulation, hyperactivity, and impulsivity. Meanwhile, individuals with ASD often experience difficulties in social communication and interaction, as well as restricted interests and repetitive behaviors [2,3]. Globally, the prevalence of persistent adult ADHD was estimated at 2.58% in 2020, corresponding to approximately 139.84 million affected adults. Similarly, the global lifetime prevalence of ASD is also high (around 1%), with affected individuals facing challenges in adulthood, including a high unemployment rate of 54% and a mortality rate 2.9 times greater than that of the general population [4].

Although various treatments are available for ADHD and ASD-including pharmacological, behavioral, and physical interventions-the underlying mechanisms of these treatments are not yet fully understood [5]. In addition, patients and caregivers may experience uncertainty when navigating treatment options, evaluating efficacy, and considering long-term outcomes [6].

To address these issues and provide a comprehensive synthesis for both patients and researchers, this review aims to offer an overview of current treatment approaches [7]. It will examine pharmacological, behavioral, physical, and other therapeutic interventions for ADHD and ASD. Finally, the review will discuss the limitations and gaps in the existing literature and propose directions for future research.

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2. Treatment's impact on ADHD symptoms

2.1. Medicine

Adrenergic neurotransmitter reuptake inhibitors, such as atomoxetine and viloxazine, serve as vital non-stimulant avenues for managing ADHD. These pharmacological agents prove especially advantageous for individuals who exhibit intolerance toward stimulants or present with comorbid cardiovascular risk factors. By modulating norepinephrine signaling within critical prefrontal cortical regions, these medications sharpen attention and bolster impulse control, all while bypassing the high abuse potential inherent to stimulant alternatives [8].

Stimulants remain the cornerstone of adult ADHD pharmacotherapy. Their efficacy in enhancing cognitive performance and behavioral regulation is well-documented, significantly boosting focus through the promotion of catecholamine release within the central nervous system's synaptic junctions. While concentrations of methylphenidate and dexedrine effectively mitigate impulsive tendencies, the intricate neural mapping of their clinical impact remains a subject of ongoing investigation [9].

Despite their clinical utility, stimulants often trigger a spectrum of side effects. Insomnia, suppressed appetite, and cardiovascular fluctuations-specifically elevated heart rate and blood pressure-are common concerns. Furthermore, the specter of dependency necessitates extreme vigilance; for individuals with a history of substance use disorders, the administration of these substances requires a high degree of clinical caution [10].

In contrast, non-stimulants operate under less stringent regulatory controls, offering a lifeline for patients at risk for stimulant-related complications. While both classes increase catecholamine levels, non-stimulants primarily achieve this by obstructing the reuptake of norepinephrine rather than forcing its release [11-13]. Tricyclic antidepressants (TCAs), for instance, show promise for adults struggling with concurrent mood disturbances, though they require consistent electrocardiogram monitoring due to potential impacts on cardiac conduction. Similarly, norepinephrine-dopamine reuptake inhibitors like bupropion mimic some stimulant effects, yet they carry risks of sexual dysfunction or seizure triggers in susceptible individuals. It is worth noting that some of these options lack formal FDA approval for ADHD, necessitating a highly specialized and cautious approach during clinical consideration [14].

Alpha-2 adrenergic receptor agonists, including clonidine and guanfacine, function by dampening sympathetic nervous system output [15,16]. While their application in adult populations is less frequent compared to pediatric cases, they are remarkably effective at addressing sleep disturbances associated with the disorder [17]. However, the trade-off often involves significant daytime drowsiness. These agents might benefit hypertensive patients due to their blood-pressure-lowering properties, yet they demand careful oversight in individuals with low or standard baseline blood pressure to avoid hypotension.

Selecting the right medication often hinges on the desired duration of the therapeutic effect [18,19]. A preference for long-acting formulations prevails among patients, largely because once-daily dosing simplifies adherence and minimizes the risk of misuse [20]. Nevertheless, long-term data for middle-aged or elderly demographics remains sparse, creating a gap in our understanding of geriatric ADHD management. Consequently, many clinicians favor a cautious titration strategy using short-acting variants. This methodical escalation typically involves a rotating schedule of low, medium, and high doses-each sustained for nearly a week-allowing for a precise calibration of symptom relief against physiological tolerance. If a specific medication category proves untenable or results in unacceptable side effects, the protocol suggests repeating the trial with a second stimulant from a different chemical class [21-24].

2.2. Behavioral treatments

When medication leaves residual symptoms or remains contraindicated, behavioral interventions step in as a robust secondary defense [25]. Cognitive Behavioral Therapy

(CBT) currently dominates this space, offering practical frameworks for improving organizational habits, focus, and emotional regulation. Structured CBT programs-focusing on ADHD education, time management, and social skills-have yielded significant improvements in comorbid anxiety and depression, proving that cognitive retraining can fill the gaps left by chemistry alone [26].

Beyond behavioral changes, CBT appears to reshape neural architecture [27]. Post-treatment observations often reveal increased resting-state functional connectivity within the fronto-parietal network and the posterior cerebellum-regions typically targeted by pharmaceutical agents. Enhancements in the superior parietal lobules and occipital lobe further correlate with tangible symptom reduction, suggesting that systematic cognitive exercises physically alter the way the brain communicates [28].

Acceptance and Commitment Therapy (ACT) provides another pathway, specifically targeting impulsivity and the psychological "fallout" of ADHD, such as academic procrastination or chronic low quality of life [29]. By reducing overactivity in the left anterior cingulate cortex and the insula, ACT helps stabilize the very regions responsible for emotional turbulence. However, clinicians must ensure the therapy doesn't become overwhelming; the linguistic complexity involved in "disengaging" from one's thoughts can be taxing for patients who already struggle with information processing [30-32].

Complementing these approaches, mindfulness practice serves to refine attention and mitigate negative affect [33]. While the exact mechanics are still being mapped, evidence suggests mindfulness might preserve neuronal health and inhibit apoptosis, fostering better self-care habits [34]. Regular practice often leads to improved diet and exercise, which in turn enhances the overall therapeutic effect. Furthermore, Dialectical Behavior Therapy (DBT) group sessions have shown a significant impact on reducing executive function disorders, with benefits that persist long after the formal treatment concludes [35,36].

2.3. Other treatments

Other treatments for adult ADHD include neuromodulation techniques, physical exercise, and music therapy. These interventions provide sophisticated alternatives for those who prefer non-pharmacological routes. Brain stimulation methods, such as transcranial direct current stimulation (tDCS) and deep transcranial magnetic stimulation (TMS), target the right or left dorsolateral prefrontal cortex (DLPFC). Home-based tDCS applications have shown particular success in improving inattention for non-medicated patients [37]. Likewise, TMS targeting the prefrontal and parietal cortices enhances working memory performance by activating the specific neural circuits responsible for executive control [38,39].

Moreover, adjunctive interventions like physical exercise and music therapy have a transformative impact. Compared to standard gym routines, specific types of movement such as Tai Chi and yoga are more effective at improving symptoms. These exercises boost cognitive functions by increasing norepinephrine and dopamine levels in the prefrontal cortex and hippocampus, essentially mimicking the biochemical effects of stimulants [40].

Similarly, music can stimulate the prefrontal cortex through rhythmic auditory cues, enhancing executive functions and alleviating self-control deficits. Music also strengthens the default mode network (DMN), a system that is often weakly connected in ADHD brains [41,42]. Interestingly, natural music and classical compositions can activate the DMN due to their complex rhythm and pitch, demonstrating the profound neural plasticity that results from long-term auditory engagement.

2.4. Combined / integrated treatments

The most widely utilized and effective strategy for adult ADHD is the integration of pharmacotherapy with behavioral support [43]. Combining stimulant medications with targeted behavioral therapies is often considered the gold standard. This synergy effectively improves attention and memory while simultaneously tackling comorbid symptoms like hopelessness or anxiety [44].

Research suggests a sequential approach: starting with medication to stabilize the brain's baseline chemistry, followed by CBT to prevent symptom relapse. Because CBT requires a certain level of foundational self-control to be effective, medication can often provide the "mental floor" necessary for the patient to engage with the therapy [45].

Beyond the standard medication-CBT pairing, the combination of DBT and tDCS has shown remarkable effectiveness, often outperforming either method used in isolation [46]. The improvement in attention likely stems from the dual impact of electrical stimulation on the DLPFC and the mindfulness components inherent in DBT. Currently, the medication-behavioral therapy duo remains the primary recommendation due to its widespread availability and the clear additive benefits that arise when physiological and psychological interventions work in tandem [47].

3. Treatment's impact on ASD symptoms

Regarding the clinical landscape of adult Autism Spectrum Disorder (ASD), we need to move beyond a simple list of interventions and instead look at how these diverse strategies intersect to support neurodivergent lives [48]. I have refined and expanded your text to ensure the tone remains professional-as if we were analyzing these findings for a high-level seminar-while meticulously stripping away the citations and polishing the prose for better rhythm and impact [49].

3.1. Medicine

Antipsychotic pharmacological agents currently serve as the primary clinical frontline for adults navigating ASD. These medications do not target the core neurological architecture of autism itself but rather modulate the dopaminergic and serotonergic systems to manage secondary behavioral challenges [50,51]. High-affinity receptor blockers such as risperidone, thioridazine, and ziprasidone remain the most frequent prescriptions. Their utility lies in their ability to dampen acute irritability and aggressive outbursts, providing a stabilizing floor for the patient [52]. However, prescribing patterns are far from universal; they shift significantly based on regional clinical protocols and the specific therapeutic philosophy of the practitioner. While these agents effectively suppress manic tendencies, the medical community remains cautious regarding the metabolic and neurological toll of multi-decade usage [53].

Loxapine offers a more targeted alternative for reducing severe aggression, yet its potent dopamine-blocking characteristics present a double-edged sword. For patients with profound physical disabilities, the risk of extrapyramidal side effects may outweigh the behavioral benefits [54].

The secondary tier of intervention involves antidepressants, with selective serotonin reuptake inhibitors (SSRIs) leading the charge. Clinical trials have demonstrated that fluoxetine can significantly attenuate the intensity of repetitive behaviors and obsessive thought patterns [55]. Interestingly, while insomnia occasionally surfaces as a side effect, the more severe psychiatric risks often associated with antidepressants in younger populations appear less prevalent in the ASD adult demographic. Other agents like sertraline show a similar efficacy profile, offering a favorable balance between symptom reduction and physical tolerance [56].

Beyond these standard categories, the pharmacological toolkit includes mood stabilizers like valproic acid and anxiolytics like buspirone, which aim to lower the social "noise" that often hinders meaningful interaction. Atypical antipsychotics such as clozapine are reserved for more destructive behavioral patterns [57]. Despite the potential for weight gain and gastrointestinal issues, many clinicians find its overall tolerance profile acceptable given the severity of the symptoms it addresses.

Psychostimulants present a more complex challenge. While they are the gold standard for ADHD, their efficacy drops sharply when applied to the core symptoms of ASD [58]. Adults on the spectrum often exhibit a heightened sensitivity to these substances; doses that would be standard for a neurotypical ADHD patient can trigger intense irritability or an increase in stereotyped movements. Consequently, a "low and

slow" titration strategy is essential to avoid gastrointestinal distress or sleep fragmentation [59].

We are also seeing a growing interest in non-traditional, nutrient-derived interventions. Sulforaphane-a compound extracted from cruciferous vegetables like broccoli-has shown promise in enhancing social responsiveness and verbal communication [60]. This is not mere supplementation; it is a targeted attempt to reverse cellular abnormalities. By addressing oxidative stress, mitochondrial dysfunction, and neuroinflammation, these low-toxicity options offer a biochemical "rebalancing" that traditional pharmaceuticals often ignore.

Ultimately, the reality of adult ASD care is one of polypharmacy. Because symptoms rarely exist in isolation, most patients navigate a complex cocktail of medications. This necessitates a holistic diagnostic approach, where the practitioner must account for the interplay between current prescriptions and the patient's unique physiological baseline.

3.2. Behavioral Treatments

Cognitive Behavioral Therapy (CBT) remains the dominant force in the behavioral landscape, though its application has evolved. Group-based CBT, in particular, has proven transformative. By providing a structured environment where individuals can articulate their experiences and deconstruct emotional triggers, these groups foster a sense of shared reality. This communal problem-solving doesn't just manage symptoms; it recalibrates the individual's self-perception, shifting the narrative from one of "deficit" to one of "management."

Modified versions of CBT, such as Social Skills Intervention (SSI), focus specifically on the paralyzing nature of social anxiety. These programs encourage participants to normalize their anxieties through shared experience and iterative skill-building. Some of the most effective interventions involve highly personalized "homework," such as making brief phone calls to fellow group members to practice real-world communication in a low-stakes setting. These adjustments prove that when the rigid structure of traditional CBT is bent to fit the autistic profile, its effectiveness surges.

Beyond cognitive restructuring, Behavioral Skills Training (BST) utilizes a more pragmatic, role-playing approach. By rehearsing appropriate social exchanges in a controlled environment before transitioning to natural settings, participants build a "muscle memory" for conversation that persists long after the training ends. Similarly, the TEACCH framework emphasizes the power of the environment. By organizing daily life into defined, predictable zones, this structured teaching approach minimizes the background anxiety that often cripples autonomy. When activities are aligned with an individual's specific interests, the resulting gains in functional communication are often profound.

More recent adoptions include Dialectical Behavior Therapy (DBT), which focuses on the four pillars of mindfulness, emotional regulation, distress tolerance, and interpersonal effectiveness. This is not just about behavior-it is about self-acceptance. Participants report a heightened awareness of their own emotional states, which allows them to navigate life's stressors without spiraling into crisis. Similarly, programs like NeuroACT combine functional context with executive function support. By teaching patients to "disengage" from overwhelming sensory or linguistic environments, these programs directly improve the overall quality of life and reduce the heavy burden of depressive symptoms.

3.3. Physical Treatments

Neuromodulation has emerged as a high-potential frontier for those seeking alternatives to traditional talk therapy or medication. Transcranial Direct Current Stimulation (tDCS) typically targets the dorsolateral prefrontal cortex (DLPFC) and the temporoparietal junction (TPJ). These areas are the hubs of social cognition and emotional regulation. By applying a low-level current, tDCS appears to correct the inherent imbalance between neural excitation and inhibition. Observations suggest that this can actually increase neuronal density and adjust neurotransmitter levels, leading to tangible improvements in language fluency and social recall.

Transcranial Magnetic Stimulation (TMS) offers another layer of precision. By utilizing magnetic pulses to regulate gamma oscillations, TMS can normalize some of the social deficits that define the disorder. Whether through repetitive pulses (rTMS) or the more naturalistic rhythm of intermittent Theta Burst Stimulation (iTBS), these interventions target the very circuits responsible for compulsive behaviors and social anxiety. While iTBS is currently more focused on attention and executive control, the potential for expanding these protocols into deeper social cognitive processes remains a primary focus of current research.

For the most severe cases-specifically those involving intractable self-harm-Deep Brain Stimulation (DBS) provides a radical but necessary option. By implanting electrodes in regions like the internal capsule or the amygdaloid nucleus, clinicians can regulate the chaotic neuronal discharge patterns that drive self-destructive urges. This is a measure of last resort, but for many, it represents the only effective way to break the cycle of obsessive-compulsive behaviors and physical harm.

3.4. Other Treatments

The therapeutic landscape for ASD extends far beyond the clinic wall. Physical exercise has proven to be an underrated but potent tool. In some cases, pre-exercise routines have managed to reduce aggressive outbursts more effectively than standard sedatives like lorazepam. The logic is simple: exercise provides a healthy outlet for excitability that a chemical inhibitor might only suppress. Customized physical activities-incorporating visual cues or game-like structures-not only lower stress but also enhance the sense of personal satisfaction and social participation.

Music therapy operates on a similar sensory level. Autistic individuals often show a heightened physiological response to self-selected music, which can act as a powerful emotional regulator. Unlike generic "relaxing" tracks, music that resonates with the individual's own aesthetic preferences can stabilize mood and provide a bridge to communicative expression.

We must also consider the role of environmental and vocational support. Employment counseling that offers "supportive" rather than "sheltered" environments has shown significant cognitive benefits. Adults who work independently with appropriate assistance often outperform their unemployed peers in spatial memory and complex problem-solving. By developing personalized workplace plans, these projects empower individuals to organize their own tasks, thereby building self-esteem and social cooperation skills simultaneously.

Art therapy and animal-assisted therapy (AAT) round out these diverse options. Whether through the structured focus of drawing portraits-which naturally encourages eye contact and the reading of facial expressions-or the calming presence of a trained animal, these therapies provide a non-threatening space for growth. AAT, in particular, has been shown to reduce depressive symptoms and enhance social awareness over relatively short periods, offering a unique form of companionship that human interaction sometimes fails to provide.

3.5. Combined / Integrated Treatments

The future of ASD care undoubtedly lies in the synergy of these methods. Early experiments combining tDCS with CBT have shown that the two are more than the sum of their parts. Electrical stimulation can "prime" the brain, making it more receptive to the cognitive strategies taught in therapy. This combined approach has yielded superior results in language comprehension and overall social integration compared to using either method in isolation.

However, we must be honest about the current state of the research. High-quality data on integrated therapies is frustratingly scarce. This gap is partly due to the high failure rate of clinical trials in the central nervous system sector and the inherent difficulty in standardizing an "ASD diagnosis" across diverse populations. Despite these hurdles, promising combinations-such as linking behavioral interventions with targeted chemical support-offer a glimpse into a more nuanced, effective future for adult ASD treatment.

We are moving toward a model where the biological, the behavioral, and the environmental are treated as a single, interconnected system.

4. Discussion

This review mainly analyzes the existing studies testing performance of interventions for adult with ADHD or ASD, including drug therapy (such as stimulant treatment for ADHD and risperidone treatment for ASD), behavioral therapy (mainly CBT), physical therapy (including tDCS, TMS, and DBS), as well as some other therapies (e.g., exercise, art, and music).

However, there are still some concerns. First, studies that assess the performance of integrated interventions are relatively scarce, with most research focusing on the combination of a few popular treatments. At the same time, more attention can be paid to some less common treatments. For example, in behavioral therapy, more focus can be placed on treatments such as mindfulness, NeuroACT, rather than just CBT. Long-term effects of those interventions can also be conducted, since many experiments only tracked the subjects for a week. Second, most of the existing treatments are targeting the children population, with relatively few studies specifically conducted on adults with ADHD or ASD. Additionally, there is a lack of treatment for core symptoms of ASD, such as repetitive behaviors, and more attention is given to co-occurring symptoms such as depression and anxiety.

At the same time, the current treatments for ADHD and ASD also have risks, inclu ding the potential for medication abuse, as the current medications used for these conditions are mainly stimulants, which are easy to bacome addicted. Secondly, many medicines have side effects. Among them, the most dangerous side effect is an increase in blood pressure. Therefore, when used by patients with hypertension, they need to be cautious. From this, it can be seen that one drawback of current medical treatment is that for patients with other coexisting symptoms, the safety of medication needs to be paid more attention to. Finally, for physical treatment, especially invasive therapy (such as Deep Brain Stimulation), greater attention needs to be paid to safety during its application to prevent any harm to the patient due to improper operation.

This review compares different interventions for treating ADHD and ASD, which can provide some priority choices or precautions for treatments for patients with ADHD and ASD of different needs, as well as their families/healthcare workers. At the same time, some relatively simple and easy-to-implement treatments, such as exercise and social training, can offer treatments for ADHD and ASD patients who want to try some niche therapies or want to make self-improvements.

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