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MIND MATTERS: UNDERSTANDING AND MANAGING ADHD – FROM INTRODUCTION TO TREATMENT

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ABSTRACT

Absence of concentration, hyperactivity, and impulsive behaviour are characteristics of Attention Deficit Hyperactivity Disorder (ADHD), a common neurodevelopmental disorder. Despite being thought of as a neurodevelopmental disorder with childhood start (ADHD) is a common and serious health conditions in adulthood. The major characteristics of ADHD are outlined in this concise review, including its complex etiology involving genetic and environmental factors, changing diagnostic standards, a range of treatment options (pharmacological, behavioral, and psychosocial), and exciting new directions for research in the future, including digital interventions and novel therapies. In order to improve assessment and intervention techniques and, eventually, improve the lives of those impacted by the illness, it is crucial to have a complete understanding of ADHD.

Keywords: ADHD, Inattention, Hyperactivity, Impulsivity, Stimulants, Non – stimulants

1. INTRODUCTION

Lack of focus, hyperactivity, and impulsive behavior are signs of attention deficit hyperactivity disorder (ADHD), a neurodevelopmental condition. Globally, prevalence of ADHD ranges from 1.2% to 7.3% in adults and from 5.9% to 7.1% in children with a frequency of more than 5%, ADHD is among the most prevalent conditions in adolescent psychiatry among children aged six to seventeen **[1]**. It is divided into three subtypes: inattentive, primarily impulsive and hyperactive, and mixed, depending on the severity of the symptoms **[2]**. These symptoms can vary in

severity and may persist into adulthood. While most studies concentrate on children between the ages of 7 and 17, it is important to take into account that adults may acquire ADHD. Furthermore, the underlying etiological mechanisms remain unclear and are likely heterogeneous and multifactorial, involving a variety of risk components including dietary, psychological, surrounding areas, perinatal, and environmental toxins **[3]**. The International Classification of Diseases, editions 10 and 11 (ICD-10/11) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) both have a set of exact criteria that must be met, which is based on observation and enlightening reports, keeps defining ADHD in terms of behavioral criteria, it is diagnosed **[4]**. It's crucial to remember that each person with ADHD presents differently; not everyone with ADHD will exhibit all three of these basic symptoms. The symptoms can be effectively treated with medication, and research indicates that early detection and treatment may enhance long-term social, vocational, and educational outcomes. **[5]**. A officially authorized healthcare provider, such as a psychiatrist or psychologist, should make a formal diagnosis of ADHD after conducting a thorough evaluation and taking the DSM-5's criteria into account **[6]**. It is a very heterogeneous disorder, despite consistently observed differences in groups between individuals who have and do not possess the disorder. Because of this, it has become very difficult for researchers to determine the pathophysiology, effective treatments that change the course of development, and the variety of consequences of ADHD, especially on an individual basis. ADHD is often diagnosed by a physician based on the severity, duration, and number of behavioral symptoms that parents and teachers have observed **[7]**. They are not described in terms of biologically recognized markers or etiological sources. The relationships between the neurobiological underpinnings, etiological causes, and clinical definitions of ADHD are still up for debate. Plenty comorbid behavioral and mental health conditions, which include oppositional disorder, mood disorders, feeling uneasy, and language disorders, and learning disabilities. These co-occurring issues may make it more difficult to diagnose and treat ADHD. ADHD also has a significant hereditary component; a study on twins revealed an estimated heritability of 70–80% **[8]**. Consequently, it is a lifelong condition. However, medical professionals who evaluate cognitive and behavioural disorders in adult populations are frequently unaware that symptoms of ADHD can still be seen. Thus, increased knowledge of Adult ADHD may result in improved handling of this kind of population, as well as medical care, since this illness causes functional

impairment in day-to-day activities **[9]**. This introduction aims to explore the potential of nano carriers in revolutionizing ADHD treatment by providing a brief overview of ADHD, current treatment approaches, and the role of nano carriers in optimizing drug delivery for enhanced therapeutic efficacy and improved patient compliance **[10]**.

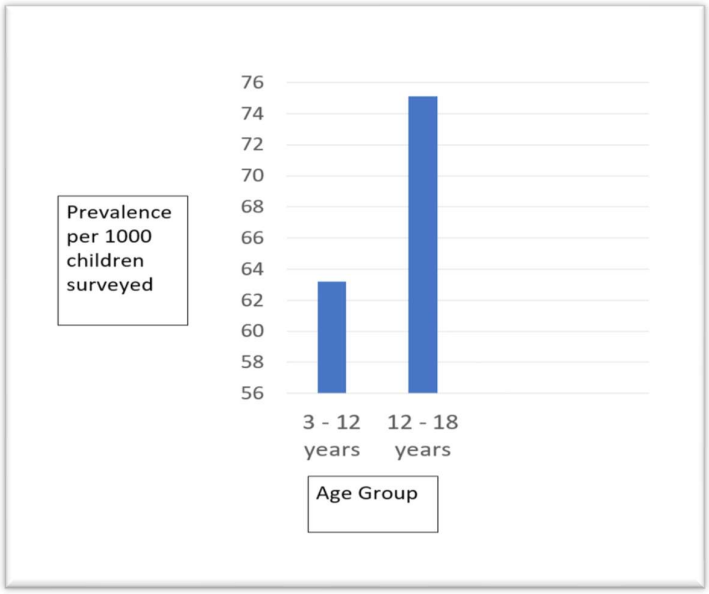

Figure 1: ADHD prevalence among children [11]

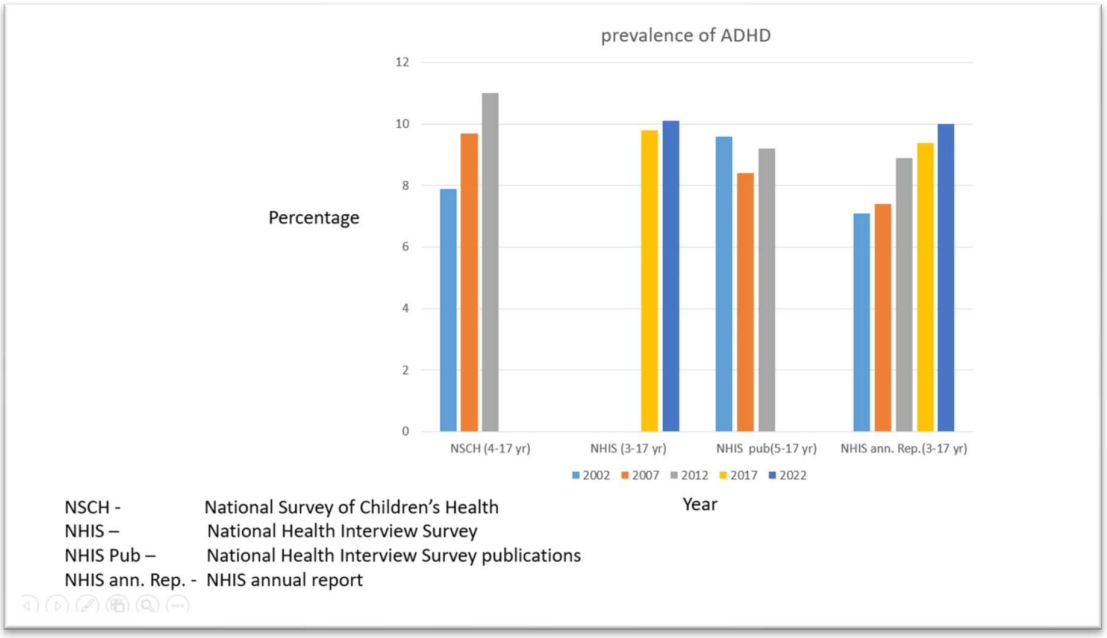

Figure 2: ADHD prevalence among children [12]

2. PATHOPHYSIOLOGY

ADHD is thought to impair the "frontal" circuitry due to weaknesses in executive cognitive processes. In adults and children with ADHD, structural imaging investigations have indicated diffuse

abnormalities **[13]**. The cerebellum, the four cerebral lobes, and the total cerebrum were all smaller in a large and did not change over time. A study of adults with and without ADHD used structural magnetic resonance imaging, which revealed decreased dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC). The DLPFC controls working memory, or the capacity to hold data when examining recently obtained data **[14]**. It is believed that these variations explain why people with ADHD display deficiencies in action that is driven by objectives and concentrated. It is believed that the ACC is a crucial area of regulation pertaining to the capacity to concentrate on a single task and make decisions **[15]**. The cortical maturation developmental pattern in ADHD is examined. According to the report, people with ADHD have a delayed cortical thickness. In both children with and without ADHD, the trajectory of brain development from sensory-motor to linked areas appeared comparable **[16]**. Those with ADHD, on the other hand, suffered a delayed developmental peak age. A study that employed identical grown-up thickness of cortex measurement came to the conclusion that Adults with ADHD still experience symptoms in the same brain regions that affected children. And that cortical thickness is not normalized. Cortical thickness assessments in the DLPFC, parietal regions, and ACC in individuals with ADHD were thinner in this study than in those without ADHD. In people with ADHD, brain activity has been observed during specific cognitive challenges using functional magnetic resonance imaging (fMRI) **[17]**. In research that makes use of neuropsychological test "go/no-go" to measure brain activity, it was discovered that individuals with ADHD, both adults and children, had reduced engagement in the front striatal brain areas (prefrontal cortex and caudate), which are important for attention and inhibitory control. Non-front striatal areas (ACC, parietal regions) were more engaged in ADHD patients compared to controls. There was a considerable link between the degree of brain activity and the task efficacy of both children and adults with ADHD **[18]**.

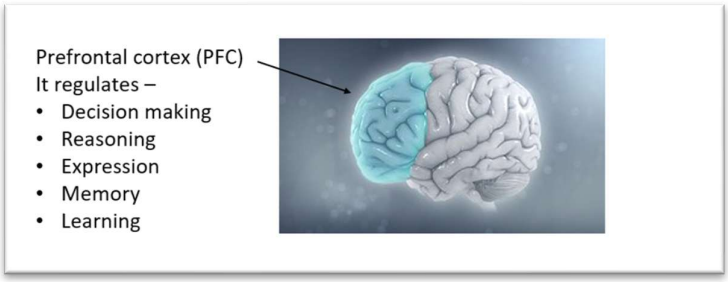

Figure 3: Prefrontal cortex [19]

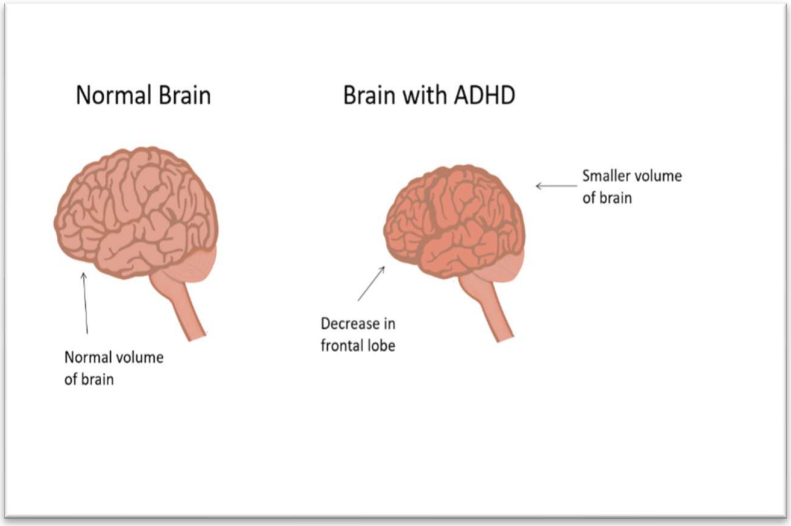

Figure 4: Normal brain vs. ADHD brain [20]

3. Symptoms-

Genetics and environmental factors are two of the many complex causes of ADHD. The illness is typically identified in children when problems occur during play and education. It is distinguished by physical unease, trouble focusing, and a limited capacity for concentration. It is usually associated with negative thinking or improper parenting. Children with this condition most likely have an underlying neurological defect explaining their behaviour, according to a brain imaging research. In other words, these children's brains are still maturing and not fully developed. Although certain key brain circuits are thought to be operating normally, cortical areas associated to attention, impulse control, and sensory integration are thought to be under activated. ADHD is a widespread disorder, and our understanding of it is continually evolving. It can be present with a range of symptoms. But the primary three types of symptoms linked to ADHD are: inattentive, mostly impulsive and hyperactive, and combination **[21-25]**.

Inattention: This group of symptoms includes inability to focus, casual errors, forgetfulness in day-to-day activities, trouble organizing chores, and unwillingness or reluctance to work on projects requiring extended mental effort. People with ADHD frequently struggle to pay attention to details and may struggle to stay on task.

Examples –

(a.) Finds it difficult to focus on tasks or play activities.

(b.) Pays little attention to details or commits thoughtless errors.

(c.) Appears not to hear when spoken to directly.

(d.) Disregards instructions and fails to complete tasks at work, school, or household chores

(e.) Has difficulty planning activities or tasks

(f.) Avoids, detests, or shows reluctance to perform tasks requiring prolonged mental strain.

(g.) Promptly side-tracked

(h.) Forgetful in day-to-day tasks

Hyperactivity- impulsivity: This category includes symptoms like fidgeting, tapping, or restlessness, as well as a difficulty remaining motionless, difficulty staying seated in circumstances where it is projected, and excessive talking. Hyperactivity is often more visible in children, whereas in adults, it can manifest as feelings of restlessness or an inner sense of unease. Symptoms of impulsivity include being unable to wait one's turn, answering questions before they are fully asked, and constantly interrupting other people. Impulsivity control issues in people with ADHD may result in rash decisions or actions that they later come to regret **[26]**.

Examples –

(a.) Engages in fidgeting, taps feet or hands, or wiggles while seated.

(b.) Rises from the chair when it is anticipated for them to stay seated.

(c.) When not appropriate, runs around or climbs (may emerge as restless feelings in adults or adolescents).

(d.) Incapable of participating in or enjoying tranquil leisure activities.

(e.) "In motion,"

(f.) Talks too frequently

(g.) Answers questions incoherently before they are fully asked

(h.) Exhibits difficulty waiting for their moment

(i.) Interferes with or bothers other people

4. Etiology-

Similar to other prevalent medical and psychiatric conditions (such as schizophrenia or asthma), ADHD is shaped by a blend of non-inherited factors, multiple genes, and the interactions between them. ADHD's precise causation is uncertain, and the disorder is not necessarily the result of being exposed to a risk factor. This means that a specific risk factor may exist in the population that is unaffected and will only be detected in a subset of cases. Furthermore, distinct risk factors may have a greater influence on the course and outcomes of ADHD than on its etiology **[27]**. Complicating matters is the possibility of genetic and environmental factors interacting to create indirect risk effects. Genes can change an individual's sensitivity

to environmental risks, such as toxic substances found in the environment or psychosocial adversity (gene–environment interaction) **[28]**. The likelihood of being exposed to specific environmental risks can also be influenced by inherited factors (gene–environment correlation). This means that the impacts of hereditary and environmental risk factors cannot be entirely separated. The body of data suggests that the genesis of ADHD is influenced by both hereditary and environmental factors **[29]**. Early beliefs of diminished brain function were based on several observations of lower gray and white matter volume or functionality in the brain. These deficiencies were connected to response time, cognitive processing, attention, motor planning, and behavioural problems attributed to ADHD. In recent times, the key areas displaying deficits in ADHD have been pinpointed as the prefrontal cortex (PFC), caudate, and cerebellum. Collectively, these areas, which are connected by a nerve network - control behaviour, emotions, thoughts, and actions as well as attention. Studies on ADHD patients have revealed smaller volumes and decreased activity in the PFC, caudate, or cerebellum, as well as slower PFC maturation. Dopamine (DA), norepinephrine (NE), and neurotransmitters (NTs) keep the network activity going in these areas, which are very sensitive to changes in the neurochemical environment and communicate with one another via a number of receptors that can be postsynaptic or presynaptic **[30]**. Dopamine D4 receptor and transporter gene (DAT1) mutations have been connected to the ADHD phenotype. Neurotransmission failure concentrated in the prefrontal cortex and linked subcortical systems is common into adulthood, as are difficulties with noradrenaline and dopamine metabolism **[31]**. The heritability of ADHD symptoms varies according to different statistics. Studies with identical siblings have shown up to 80% correlation, with fraternal twins showing up to 32%, and closest relatives showing up to 25% **[32]**. Multiple research investigations have shown that ADHD patients have lower-than-normal DA receptor density in various brain regions **[33]**. ADHD is associated with a range of environmental events that take place during different phases of the development of the central nervous system (CNS), including the perinatal and gestational eras **[34]**. Environment-related variables also have an impact on the aetiology of ADHD, such as prematurity, poor quality early caregiving, perinatal complications, stress and smoking among pregnant mothers. Nevertheless, there is insufficient data to conclude that children with ADHD symptoms who are raised in chaotic environments differ significantly from kids from stable homes **[35]**. Certainly, it is not appropriate to rule out an ADHD diagnosis upon the grounds

that, "This children's hyperactivity makes sense—everyone would be experiencing this kind of family chaos" **[36]**.

5. Diagnosis of ADHD-

GPs, or general practitioners, are essential in the early detection of potential cases. GPs make the majority of referrals to the specialized services, even though the diagnosis of ADHD can only be made by an individual's health professionals. General practitioners also have a distinct advantage in identifying possible cases because they have a large reference group to work with and have seen hundreds of children in their practice **[37]**. It's likely that teachers will identify ADHD children in a similar way. However, parents frequently lack the advantage of having a sizable reference group to which they can compare their child. The idea of discovering a diagnostic marker for ADHD has been examined in various imaging investigations; however, this potential has yet to be fulfilled, possibly due to the disorder's complexity **[38]**. When diagnosing ADHD, clinicians adhere to the recommendations in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). However, given that ADHD has three distinct subtypes, every one with a unique set of symptoms, and diagnosing a specific subtype of ADHD requires a child to display a minimum of six symptoms (five for those over 17) consistently for at least six months. Additionally, there must be observable functional impairment in various contexts **[39]**. The accuracy of an ADHD diagnosis is challenging due to the reliance on these arbitrary criteria. While the DSM-V ADHD criteria are an improvement over the DSM-IV-TR criteria, they still fall short of effectively addressing the issue of gender variations in ADHD **[40]**. The age range of typical primary care presentations varies. Young children may exhibit short play periods (less than three minutes), abandoning tasks, not seeming to be listening, moving almost constantly, and displaying no fear of danger. Primary school-aged children often exhibit the inability to focus for longer than ten minutes when engaged in moderately difficult activities, changing activities too soon, and seeming disoriented, forgetful, and distracted by their surroundings. They also frequently act out of turn, interrupt other kids and respond without thinking, become agitated when composure is expected, and disregard the rules **[41]**. Lastly, older kids and teens frequently show up less persistently than their counterparts (less than thirty minutes), a lack of attention to task details, inadequate preparation, restlessness, a lack of self-control, and careless risk-taking **[7]**. Routine screening for ADHD is

advisable in adult and elderly individuals who present cognitive and/or behavioural concerns when seeking assistance from neurology, psychiatry, or geriatric departments. This is crucial because neurological and psychiatric conditions might mask the diagnosis of ADHD, which can go undetected in childhood and manifest in adulthood **[42]**. However, geriatricians, neuropsychologists, psychiatrists, and neurologists who specialize in treating older adults may not always be familiar with managing neurodevelopmental disorders like ADHD in adults. Furthermore, children with ADHD are often neglected during their transition to adulthood, despite the fact that they require specialized healthcare services, even after an ADHD diagnosis **[43]**. Adults with ADHD have a difficult time getting a diagnosis because the neurodevelopmental disorder is based on lifelong anamnestic evaluation, including symptomatology specific to children, that extend beyond DSM-V listed items **[44]**. Adult ADHD must be diagnosed methodically because it is a complicated diagnosis. Because adults and their informants have difficulty recalling the start of symptoms in hindsight, discussing childhood symptoms subsequently should be done with caution in the absence of documented facts. Using objective data, such as school reports, can help provide a more trustworthy assessment of previous symptoms **[45]**. A favourable family history of ADHD is often supportive of a verified diagnosis of the illness. Physicians should discuss the diagnosis process, the patient's current symptoms, and the required course of therapy with patients who have previously received an ADHD diagnosis. Rating scales should be part of the medical record since they are a helpful tool for monitoring progress and making adjustments to treatment plans **[46]**.

6. Treatment of ADHD-

Medication, behavioural therapy, or a mix of the two can be used to treat ADHD. Treating children with ADHD, regardless of approach, is recommended since evidence shows that treating the illness early on can enhance results, lessen issues as adults, and reduce the strain on parents and educators **[47]**. In the early stages, several psychologists suspected that poor parenting was a factor in ADHD, encouraging the creation of numerous behavioural treatments for the illness. However, not every patient responded favourably to these approaches. It was believed that medication therapy was superior to behavioural therapy in the wake of evidence supporting a neurochemical basis for ADHD. Many doctors combined behavioural therapy with medication therapy; however, it was unclear how beneficial it was to combine the two treatments, how effective behavioural therapy was in comparison to medication therapy, and how beneficial either approach

would be in the long run **[48]**. These problems were simultaneously addressed by a ground-breaking study called the Multimodal Treatment Study of Children with ADHD (MTA). When addressing the symptoms and manifestations of ADHD, medication therapy has been demonstrated to be more effective than behavioural therapy **[49]**. Furthermore, even though all techniques studied in the study exhibited a persistent benefit, the two did not combine to provide a cumulative impact. Although behavioural therapy provided some benefits, its long-term impact did not match that of pharmaceutical therapy. Conversely, a number of studies have shown that behavioural therapy has advantages comparable to those of low-dose stimulants **[50]**. Because of this, it might work well for those with ADHD who have minimal symptoms and little impairment, or if parents would rather use it instead of medication therapy. Additionally, behavioural treatment may be used in conjunction with pharmacological therapy when there are concurrent comorbid disorders or when a partial response to FDA-approved drugs is noted. The FDA has approved a number of drugs to treat ADHD, including nonstimulants (considered alternative agents) like atomoxetine and extended-release -2 agonists like guanfacine and clonidine, as well as stimulants (considered first-line agents) like amphetamines and methylphenidate. Off-label usage of tricyclic antidepressants (TCAs), agonists, immediate-release -2 agonists, and bupropion for the treatment of ADHD has been documented. These choices are often saved for situations where the medications on the previous list are ineffective or unusable **[51]**.

7. Pharmacological treatments –

- Stimulants –

Two stimulant-based treatments that the FDA has approved for use in all age groups in the US are amphetamines and methylphenidate. However, many individuals need more than the maximum daily amount allowed by the FDA to have the desired effect, which is why these medications are categorized as off-label. However, there is a lack of evidence about the effectiveness and safety of these higher doses **[52]**. By interacting with and blocking the dopamine transporter (DAT-1) and the norepinephrine transporter (NET), stimulants decrease the absorption of dopamine (DA) and norepinephrine (NE). Amphetamine can also enter the presynaptic terminal via DAT-1 and NET to release stored NTs. The monoamine oxidase enzyme, which breaks down catecholamine's, is inhibited by both stimulants. But when it comes to this inhibition, amphetamine works better than other stimulants. Consequently, the overall

result of any stimulant is to adjust the concentrations of neurotransmitters (NTs), such as dopamine (DA) and norepinephrine (NE), at the synapses. Amphetamine and methylphenidate have slightly different modes of action, which explains why some people who respond poorly to one stimulant may respond well to the other. Long-term ADHD treatment has shown that methylphenidate and amphetamines work just as well **[53]**. Because long-acting formulations include a danger of overdose, it is best to give younger children immediate-release versions, which come in smaller doses **[54]**. Methylphenidate and amphetamines are listed as the twelfth and sixth chemicals that are known to cause physical harm, whereas tobacco and alcohol are listed as the eleventh and fourteenth, respectively. Furthermore, they are placed eighth and thirteenth, respectively, among chemicals known to create dependence, with cannabis and LSD coming in at eleventh and fourteenth. This has led to a significant deal of debate and concerns around stimulant usage, which can occasionally become a lifelong habit **[55]**. Treatment for ADHD also reduces drug addiction disorders because there is a neurological commonality between substance abusers and people with ADHD, according to imaging studies. It has been demonstrated that treating ADHD patients with stimulants reduces their aggressive and antisocial conduct. It also reduces the risk of major depressive disorder (MDD), anxiety disorders, and oppositional defiant disorder (ODD). Nevertheless, Given that at least 25% of adults and adolescents have reported engaging in these behaviour's in a survey, it is imperative to ensure that patients or their caregivers realize the value of taking these medications as prescribed. To stop drug addiction and diversion, understanding of this problem is necessary **[56]**.

- Non stimulants -

While stimulants are seen to be the best therapies for ADHD, it's important to remember that about 30% of patients may not gain much from using these drugs. In the treatment of ADHD, nonstimulant alternative medicines might be required to replace or enhance stimulants. This is particularly true in situations where there is a family history of abstaining from controlled substances, when there is a lack of responsiveness to stimulants or only partial responsiveness to them, when there is intolerance to their side effects (like insomnia), and when there are medical conditions like tic, cardiovascular, or psychiatric disorders present **[10]**. As nonstimulant treatments for treating ADHD, the FDA has approved atomoxetine (Strattera), as well as the extended-release α-2 agonist guanfacine (Intuniv) and clonidine (Kapvay) **[57]**. Despite the dearth of

carefully regulated head-to-head comparison studies, numerous meta-analyses repeatedly demonstrate that stimulants methylphenidate in particular are more beneficial than nonstimulants atomoxetine, for instance. Different study methodology and outcome measures employed in the meta-analyses may have contributed to some variation in the conclusions, even if some studies and meta-analyses have determined that these two medications are not less effective than the other. It is argued that nonstimulants usually take a few weeks to completely display their effects, which may account for the bias toward stimulants in most research, which are usually short-term **[58]**. The specific mechanism of action of guanfacine and clonidine, two alpha-2-adrenergic agonists used to treat ADHD, is yet unknown. Low and high noradrenaline secretion can potentially cause disruptions in cognitive performance. Therefore, it has been hypothesized that altering the locus ceruleus' receptiveness to sensory inputs may be related to how well alpha-2-agonists reduce the symptoms of ADHD. By inhibiting tonic noradrenergic activity and boosting locus ceruleus neurons' evoked responses by activating presynaptic alpha-2-autoreceptors, this modulation is accomplished. Moreover, these agonists may directly activate postsynaptic alpha-2-receptors in the prefrontal cortex and/or posterior parietal cortex **[59]**.

8. CONCLUSION

In conclusion, the comprehensive study of Attention Deficit Hyperactivity Disorder (ADHD) highlights the complexity of this common neurodevelopmental condition. Examining the etiology, history, symptoms, diagnosis, comorbidities, and available treatments for ADHD, the findings demonstrate the significant impact the disorder has on individuals of all ages Comorbid illnesses, such as depression and anxiety, must be addressed concurrently. Treatment methods combine behavioural therapies, psychoeducation, and medication, emphasizing the importance of tailored care. To sum up, this review highlights the need for ongoing research, awareness, and support in order to fully address the challenges posed by ADHD and enhance the lives of those affected by this condition.

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