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Brief overview about attention deficit hyperactivity disorder

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Abstract: **Background:** Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that is characterized by symptoms of inattention and/or hyperactivity/impulsivity that are developmentally inappropriate. The current diagnostic criteria for ADHD, as outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) require the presence of at least 6 symptoms of inattention and/or 6 symptoms of hyperactivity/impulsivity for a minimum of 6 months, before the age of 12, and must impair function across multiple settings. Throughout the lifespan, attention-deficit/hyperactivity disorder (ADHD) is frequently comorbid with other psychiatric and somatic disorders, although the pattern of comorbidity changes over time (Franke et al., 2018). The most prevalent psychiatric comorbidities in childhood are other neurodevelopmental disorders (NDDs), such as autism spectrum disorders (ASD) (65–80%) and learning disorders (over 45%) as well as externalizing conditions, including oppositional defiant disorder (ODD) (50–60%), and conduct disorder (CD) (20–50% in children and 40–50% in adolescents). The diagnosis of ADHD should be taken into consideration in patients who are four years of age or older and exhibit symptoms such as poor attention, distractibility, hyperactivity, impulsiveness, poor academic performance, or behavioral problems at home or school. The typical age range for diagnosis of ADHD is between six and nine years of age. The evaluation of ADHD usually starts with a comprehensive clinical evaluation includes a history and physical examination, review of information across home and community settings & application of the Diagnostic Statistical Manual of fifth revision (DSM-5) diagnostic criteria. The clinician is expected to assess the presenting concerns and use validated scales. Methods of treating ADHD can be classified into two main categories: pharmacological and non-pharmacological. The former includes stimulants, which are the first-line treatment for ADHD, non-stimulants, and other approved or unapproved drugs. The latter two groups are used when stimulants are not effective or well-tolerated. Non-pharmacological methods have also been extensively studied and can be divided into three main domains: psychological methods, complementary and alternative medicine, and devices

Keywords: attention deficit hyperactivity disorder

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that is characterized by symptoms of inattention and/or hyperactivity/impulsivity that are developmentally inappropriate. The current diagnostic criteria for ADHD, as outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) require the presence of at least 6 symptoms of inattention and/or 6 symptoms of hyperactivity/impulsivity for a minimum of 6 months, before the age of 12, and must impair function across multiple settings **(1)**.

ADHD can have a negative impact on one's social and personal life, leading to many undesired outcomes, such as educational underperformance, unemployment, and involvement in criminal activities. ADHD is now considered among the most diagnosed chronic psychological disorders in children **(2)**

ADHD is typically diagnosed in childhood, with a prevalence of 3-6% in children and adolescents. ADHD is often a persistent condition, with approximately 15% of affected children continuing to meet full diagnostic criteria by early adulthood, and an additional 50-70% continuing to experience impairing symptoms. The remittance of symptoms with age, particularly hyperactivity/impulsivity, is one reason for the lower prevalence of ADHD in adults, which is estimated to be 2.5% **(2)**

ADHD is more common in males than females during childhood, with a 4:1 ratio observed in clinical studies. However, sex differences in adults are minor. The observed gender disparity in clinical samples of ADHD is hypothesized to be partially attributed to referral bias, whereby males are more likely to be referred in childhood due to hyperactivity and behavioral issues, while females are more likely to seek treatment in adulthood. **(3)**.

Despite being one of the most studied psychiatric disorders, the exact cause of ADHD is still unknown and complex **(1)**.; however, the interplay between genetic and environmental factors provides an explanation for the development of complex disorders such as ADHD and the varying susceptibility of children to environmental risks. Furthermore, genes and environments may overlap, as genes can influence the quality of the environment, such as parenting, while environmental factors can impact gene expression **(4)**.

Regarding the pathogenesis of ADHD, it is not definitively known. However, it is suggested that a genetic imbalance of catecholamine metabolism in the cerebral cortex may play a primary role. This is supported by evidence from structural and functional brain imaging, animal studies, and the response to drugs with noradrenergic activity such as methylphenidate. **(5)**

Risk factors**Parenting factors:**

The quality of parenting and family environment are considered risk factors for attention-deficit/hyperactivity disorder (ADHD) due to their influence on a child's development and behavior. Adverse parenting practices are frequently observed in families of children with ADHD. Additionally, ADHD is a heritable disorder, which increases the likelihood that parents attending clinics with their children may also have ADHD themselves, and their symptoms are likely to impact their parenting skills. However, it remains unclear to what extent adverse parenting practices are causal factors or simply a reaction to ADHD symptoms **(6)**.

Adverse childhood experiences

Exposure to adverse childhood experiences (ACEs) such as physical or emotional abuse, chronic neglect, chronic family hardship or mental illness, or community violence can lead to a prolonged stress response ("toxic stress") that has been shown to disrupt early brain development and cause permanent changes in brain architecture and subsequent neurodevelopment. Children exposed to ACEs are at higher risk for developing ADHD as well as other psychopathology. Additionally, the impact of childhood deprivation and neglect on adult neuropsychological functioning is associated with long-lasting effects on cognitive and socioemotional development, ADHD symptom persistence, and increasing the risk of ADHD and other mental health problems. **(7)**

Maternal Factors

Maternal inflammation during pregnancy, smoking throughout the first trimester, obesity and maternal depressive symptoms appear to enhance the risk of developing ADHD. Moreover, offspring who were exposed to maternal hypothyroxinemia exhibited greater ADHD symptomatology than those who were not exposed. Exposure to neonatal asphyxia has been found to cause brain damage. Hypoxia can lead to persistent abnormalities in the dopaminergic system and even decrease the expression of the dopamine D2 receptor, thereby elevating the likelihood of developing ADHD. (8)

Prematurity/Low birthweight

Low birthweight (LBW) has been identified as a risk factor for ADHD. Children born pre-term, who are likely to have LBW, have been found to be at a higher risk of being diagnosed with ADHD, particularly the inattentive subtype, with a four-fold increase in risk reported in some studies (6). However, **Heinonen and colleagues (9)** found no association with pre-maturity and later symptoms of ADHD, but the LBW increase the ADHD risk 3 times compared with children of average birth weight.

Exposure to Environmental Pollutants

Exposure to certain organic acids, for example, Perfluorooctanoic acid (PFOA) during pregnancy has been associated with an increased risk of ADHD. Perfluorooctanoic acid (PFOA) is widely used in various products, including frying pan coatings, non-stick food packaging polishes, paints, cleaning products, and fire-fighting foams. The primary source of exposure to PFOA is through the consumption of contaminated food, particularly fish and processed meats. (10)

Diet

Dietary factors (food additives (5), sugar, food sensitivity, essential fatty acid deficiency, iron, and zinc deficiency generally do not impact behavior to a clinically significant level and do not account for most cases of ADHD (1).

However, a small subset of children may demonstrate mild adverse behavioral effects in response to dietary influences, so NICE guidelines indicate that referral to a dietician may be warranted if only perceived links between specific foods or beverages and behavior are corroborated with a food diary. (11)

Comorbidities:

Throughout the lifespan, attention-deficit/hyperactivity disorder (ADHD) is frequently comorbid with other psychiatric and somatic disorders, although the pattern of comorbidity changes over time. The most prevalent psychiatric comorbidities in childhood are other neurodevelopmental disorders (NDDs), such as autism spectrum disorders (ASD) (65–80%) and learning disorders (over 45%), as well as externalizing conditions, including oppositional defiant disorder (ODD) (50–60%), and conduct disorder (CD) (20–50% in children and 40–50% in adolescents. Mood disorders: depression (16–26%), BAD (11–75%), and anxiety disorders (10–40%) are frequently comorbid with ADHD throughout the lifespan, while substance use disorders (SUD) and personality disorders become more prevalent during adulthood. A recent systematic review has found that obesity, sleep disorders, and asthma are well-documented somatic comorbidities of ADHD in adulthood. Additionally, current research indicates that children, adolescents, and adults with ADHD have an increased risk of various somatic disorders, including diabetes, hypertension, certain autoimmune and inflammatory disorders, infections, migraine, and epilepsy (12)

Studies based on nationwide register data in Denmark and Sweden have reported increased mortality rates in individuals with ADHD. Although the observed absolute risk was small (0.3-0.5%), the relative risk of premature death in ADHD was found to be significantly higher than in the general population, and this was largely explained by unintentional injuries and suicide. It is noteworthy that treatment can reduce the risk of many negative outcomes associated with ADHD (4).

Management:

Clinical presentation:

The diagnosis of ADHD should be taken into consideration in patients who are four years of age or older and exhibit symptoms such as poor attention, distractibility, hyperactivity, impulsiveness, poor academic performance, or behavioral problems at home or school. The typical age range for diagnosis of ADHD is between six and nine years of age. **(13)**

Evaluation:

The evaluation of ADHD usually starts with a comprehensive clinical evaluation includes a history and physical examination, review of information across home and community settings& application of the Diagnostic Statistical Manual of fifth revision (DSM-5) diagnostic criteria. The clinician is expected to assess the presenting concerns and use validated scales. It is necessary to obtain information about medical and neurodevelopmental health in relation to the individual's education and psychosocial status and impairment **(13)**.

Diagnosis:

The diagnostic process for ADHD does not rely on a single specific test, and instead, the DSM-5 mandates the presence of an adequate number of core symptoms and functional impairment to establish a diagnosis. **(1)**.

The DSM-5 criteria:

DSM-5 requires the presence of a sufficient number of core symptoms and functional impairment **(1)**. There are three main ADHD presentation types, which are based on the prevalence of inattention or hyperactivity-impulsivity symptoms according to the Diagnostic Statistical Manual of fifth revision (DSM-5): predominantly inattentive type (ADHD-I), predominantly hyperactive-impulsive type (ADHD-H), combined type (ADHD-C) **(1)**.

The change in nomenclature from "subtypes" in DSM-IV to "presentations" in DSM-5 reflects the increasing evidence that symptoms of ADHD are often fluid within individuals across their lifespan, rather than stable traits. The use of "presentation" terminology better reflects the idea that the symptom profile represents the person's current symptomatology, which may change over time. **(14)**

Rating scales:

According to **Parker et al. (15)**, several scales are commonly used in clinical practice to assess ADHD. These include Conner's Parent Rating Scales-Revised, Conner's Teacher Rating Scale, Child behavior checklist, Swanson, Nolan, and Pelham-IV (SNAP-IV) Questionnaire, ADHD Rating Scale-IV, Vanderbilt ADHD Rating Scale, and ADHD Symptom Rating Scale.

Different age groups**Preschool-aged children:**

ADHD has been traditionally conceptualized as a neurodevelopmental condition with an early childhood-onset and a steady course with limited remission. While **Christner et al. (16)** have noted that ADHD cannot be reliably diagnosed in children younger than 4 years due to the difficulty in determining whether symptoms are beyond the expected behavior for the developmental age, **Shephard et al., (17)** have reported that ADHD can, in fact, be reliably diagnosed during the preschool period. During this period, hyperactivity and impulsivity are typically the most prominent symptoms, and some neurocognitive deficits associated with the disorder are already detectable.

The most diagnosed presentation in preschool children is the hyperactive-impulsive (2.8%), followed by the combined (2.1%) and the inattentive (0.1%) **(13)**

Older children:

Kieling et al. (18) have reported that for most individuals diagnosed with ADHD, symptoms and impairment first appear during early childhood, even if their first formal diagnosis is made later in life.

Patients with primarily hyperactive-impulsive or combined types may present with behaviors considered as problematic before those with primarily inattentive features. Patients with the primarily inattentive type may not present until academic requirements become greater (e.g., by the fourth grade). A co-morbid learning disorder should be considered if academic progress is poor **(18)**.

Adolescents:

The observable symptom levels of ADHD tend to decline across the life course from childhood onwards in the general population. However, despite this decline, most individuals diagnosed with ADHD in childhood still exhibit symptoms and/or impairments that are sufficient for a diagnosis in adolescence and early adulthood (4).

Adult-onset ADHD:

Data from various countries have challenged the notion that ADHD is exclusively a childhood-onset condition. These studies suggest that some individuals may develop ADHD during adolescence or early adulthood, which is referred to as a late-onset variant of the condition. However, there is a dispute regarding the exact prevalence rates of late-onset ADHD, with estimates ranging from approximately 30% to 87% of those diagnosed with ADHD in adulthood, as reported by **Breda et al. (19)**.

According to **Asherson and Agnew-Blais (20)**, individuals with the late-onset variant of ADHD may differ from those with childhood-onset ADHD in significant ways. They may have less severe symptoms, a lower genetic liability for ADHD, come from more supportive families during childhood, have higher IQ, or a combination of these factors. These new findings on late-onset ADHD suggest that clinicians should consider the possibility of an ADHD diagnosis in adulthood, even if the individual did not meet the clinical thresholds for inattentive and/or hyperactive/impulsive symptoms and/or impairment during childhood.

Treatment:

Treatment of ADHD may involve a range of interventions, including behavioral, medication, school-based, or psychological interventions, either alone or in combination. The decision-making process regarding the choice of therapy should involve the patient (if at least school-aged) and their caregivers. Together with the treating clinician, the patient and caregivers must evaluate the risks and benefits of the various treatment options to determine the optimal treatment strategy. (20)

preschool children

Regarding initial therapy for preschool children (age 4 through 5 years) who meet the diagnostic criteria for ADHD, parent (caregiver) training in behavior management (PTBM; also known as behavior therapy) is recommended rather than medication. Behavior therapy can be administered by the caregivers or teachers following consultation with a behavioral therapist.

Regarding the addition of medication to behavior therapy, it may be indicated if target behaviors do not improve with behavioral therapy alone and the child's function continues to be impaired. Examples of situations where medication may be considered: expulsion (or threatened expulsion) from preschool or daycare. significant risk of injury to self, other children, or caregivers. strong family history of ADHD. suspected or established central nervous system injury (e.g., prenatal alcohol or cocaine exposure). ADHD symptoms interfere with other needed therapies. When medication is necessary for preschool children, methylphenidate is preferred rather than amphetamines or nonstimulant medications. (21)

School-age children and adolescents

For most school-aged children and adolescents (≥ 6 years of age) who meet the diagnostic criteria for ADHD and specific criteria for medication, it was suggested to initiate treatment with stimulant medication combined with PTBM (behavior therapy) to improve core symptoms and target outcomes (21) However, nonstimulant medications may be more appropriate for certain children. Comorbid conditions must be considered in selecting a specific treatment approach (22)

Adults with ADHD

Stimulant medication (eg, amphetamines or methylphenidate) is recommended as first line pharmacological treatment rather than nonstimulant medications such as atomoxetine. Stimulant medication and CBT targeting executive dysfunction have been reported to be effective treatments for ADHD in adults. Combination of both medications and CBT have added benefit for the core symptoms and outcomes (23)

Treatment modalities:

Methods of treating ADHD can be classified into two main categories: pharmacological and non-pharmacological. The former includes stimulants, which are the first-line treatment for ADHD, non-stimulants, and other approved or unapproved drugs. The latter two groups are used when stimulants are not effective or well-tolerated. Non-pharmacological methods have also been extensively studied and can be divided into three main domains: psychological methods, complementary and alternative medicine, and devices. **(1)**.

1) Pharmacological interventions:

a) Psychostimulants:

- Norepinephrine and dopamine reuptake inhibitors (methylphenidate hydrochloride, lisdexamfetamine dimesylate, dextmethylphenidate hydrochloride, etc.)

b) Non-stimulants:

- Alpha2 adrenergic receptor agonists (guanfacine, clonidine)
- Selective noradrenaline reuptake inhibitor (atomoxetine and viloxazine)

c) Other drugs used in ADHD:

- Antidepressants (bupropion hydrochloride, venlafaxine hydrochloride, desipramine hydrochloride, etc.)
- Antipsychotics (risperidone, aripiprazole, olanzapine, etc.)

(24)

Medications, with or without psychosocial interventions, are the first line therapy for school-aged children (≥ 6 years) and adolescents who meet diagnostic criteria for ADHD **(21)**

Pharmacological interventions are effective in reducing core symptoms of ADHD in most children. Among these interventions, psychostimulants such as methylphenidate, dextroamphetamine, and mixed amphetamine salts (e.g., dextroamphetamine/amphetamine) are considered the most effective option and are therefore recommended as the first-line treatment for ADHD. Although atomoxetine and alpha-2 receptor agonists (e.g., guanfacine, clonidine) have also been found to be effective, they are generally less effective than psychostimulants.

There are several reasons why a second-line drug may be considered for the treatment of ADHD. These include a strong family preference for a non-stimulant medication, concerns about drug diversion (although some long-acting stimulants can reduce this risk), or the presence of co-morbid conditions (e.g., anxiety or tic disorder).

(21)

According to the U.S. FDA, there are 12 drugs that have been approved for the treatment of ADHD. These include methylphenidate hydrochloride, methylphenidate transdermal system, lisdexamfetamine dimesylate, amphetamine sulfate, dextmethylphenidate hydrochloride, dextroamphetamine sulfate, mixed amphetamine hydrochloride/serdexmethylphenidate salts, dextmethylphenidate chloride, atomoxetine, guanfacine hydrochloride, clonidine hydrochloride, and viloxazine. **(22)**

a) Psychostimulants:

Psychostimulants affect the dopaminergic pathways in the central nervous system, which leads to a reduction in symptoms and improvement in academic performance. **(22)**. Contrary to popular belief, the use of stimulant medication does not increase the incidence of substance abuse, rather it protects against it. Approximately 70% of patients respond to the first stimulant medication, and 90% to 95% respond to a second stimulant. **(16)**.

Methylphenidate is the medication that is most supported for use in children and adolescents where amphetamine is more efficacious and acceptable than placebo in adults.. This data also perfectly correlates with information from NICE guidelines, which ranks methylphenidate over amphetamines in children and adolescents. Adverse effects of stimulant medication are generally dose-dependent and may include reduced appetite, abdominal discomfort, headache, irritability, anxiousness, and sleep problems. However, these side effects may attenuate with time or reverse after discontinuation of treatment. **(16)**.

Although depression and suicidal ideation are rare, family members should be informed about the risk. Small increases in heart rate and blood pressure have also been observed, but significant elevations are rare. The

evidence regarding whether stimulants increase the risk of cardiac problems is conflicting, so national guidelines recommend that physicians consider ECG or cardiology referral before initiating psychostimulants in patients with a history of heart disease, palpitations, syncope, or seizures, or with a family history of cardiac problems (23).

Psycho-stimulant dosing should start low and increase once to twice weekly according to feedback. Long-acting preparations have the advantage of less frequent dosing but more expensive. Tic and Tourette syndrome symptoms affect about 20% of patients with ADHD. Although stimulant use does not clearly worsen tics, it may do so in individual cases. Treatment with atomoxetine or the addition of an alpha-1 receptor agonist may improve co-morbid tics (24).

b) Non-stimulants:

Atomoxetine: Atomoxetine is a non-stimulant medication that affects noradrenergic systems. It is FDA approved for treatment of ADHD in children > 6 years old and adult. Atomoxetine may also be effective for co-morbid mood or anxiety disorders and has no abuse risk. The onset of treatment effect may be days to weeks, and optimum effect may not be achieved at 4-6 weeks. Adverse effects include somnolence, gastrointestinal upset/nausea (particularly if the dose is advanced too quickly), and reduced appetite. (21)

Although no suicides occur in clinical trials, it is recommended to monitor patient closely for suicidal thinking and behavior, clinical worsening, or unusual changes in behavior (25)

Alpha-2 receptor agonists: These antihypertensive agents are also beneficial as alternatives or adjuncts to stimulant treatment for ADHD. Potential advantages of Guanfacine over Clonidine include a longer half-life and fewer sedative and hypotensive effects. Both are useful in combination with stimulants for patients who have ADHD and co-morbid sleep problems, tics, or Tourette syndrome (21)

Viloxazine:

Regarding recent developments in ADHD medication, in 2021, the United States Food and Drug Administration (USFDA) approved viloxazine extended-release (ER) capsules (SPN-812) to treat ADHD in pediatric patients between 6 and 17 years of age. The precise mechanism of action of viloxazine is not known, but it is claimed to act by inhibiting norepinephrine reuptake. Viloxazine increases serotonin and norepinephrine levels in the prefrontal cortex and causes a minimal increase of dopamine levels in the nucleus accumbens, making it a novel drug for ADHD with the least abuse potential. Viloxazine is mainly metabolized by CYP2D6, UGT1A9, and UGT2B15 enzymes, and most of the drug has got renal elimination. Liver function tests, complete blood count and drug screening (in all patients with a history of chemical abuse or suspected chemical abuse) should be done before starting medication. Liver function tests may be indicated before beginning stimulant therapy if the patient has a history of hepatic dysfunction. Amphetamines, methylphenidate, Atomoxetine, and tricyclic antidepressants are metabolized hepatically and excreted mainly in urine (26).

MONITORING

Physician follow-up is recommended one month after initiating treatment. Height, weight, heart rate, blood pressure, symptoms, mood, and treatment adherence should be monitored at follow-up visits. Monthly visits may be required until medication dosing and timing are optimized. When an acceptable regimen is determined, follow-up is recommended at least every three months during the first year, and two or three times per year thereafter to assess control of symptoms, treatment adherence, and the presence of co-morbid conditions. Medication holidays are unnecessary unless adverse effects (e.g., decreased growth velocity) are a concern (21)

c) Off label medications:

Other medications have been used for ADHD treatment, including antidepressants (e.g., bupropion), atypical antipsychotics (e.g., risperidone, aripiprazole), and mood stabilizers. However, it is important to note that these medications are not approved by the U.S. FDA for treating ADHD and are used off-label only when first-line medications are ineffective or for the treatment of co-morbid conditions. (21)

Non-pharmacological interventions:

psychological:

- Behavior management interventions (parent training, classroom interventions, peer-based interventions, cognitive behavior therapy, classical contingency management, organizational skills intervention, social skills training, etc.)
- Cognitive training interventions (neurofeedback, cognitive training, working memory training, attention training, etc.)
- Psychoeducation

(24)

complementary and alternative methods:

- Supplementary interventions and dietary interventions (polyunsaturated fatty acids, vitamins, minerals, amino acids, herbal treatment, homeopathic treatment, etc.)
- Mind-body interventions (meditation, Yoga, Tai chi, mindfulness, hypnotherapy, massage, acupuncture, chiropractic, and osteopathic manipulation, physical activity, etc.)

(24)

Psychological:

Regarding the use of psychosocial interventions for ADHD, there are several reasons to consider them as a management option. These include concerns about the long-term efficacy of stimulant medication, limited clinical benefits of medication, non-responsiveness or weak responsiveness to medication, intolerance to medication, the clinical needs of younger children, and ethical or other objections to the use of medication. **(25)**

a) BEHAVIORAL MANAGEMENT INTERVENTIONS

Regarding the effectiveness of behavioral treatment for ADHD, longer-term analyses suggest that it provides additional benefits beyond medication alone. This is particularly true for treatment satisfaction among parents and teachers **(21)** Effective behavioral therapies include parent training, classroom management, peer interventions, and combinations of these interventions **(21)**.

I. Parent training interventions:

Behavioral parent training (BPT) is an evidence-based intervention for the treatment of ADHD and related disruptive behavioral disorders of childhood. Among children aged ≤ 5 years, the number and quality of studies demonstrating effectiveness is higher for parent behavior training than for ADHD medication **(26)**

BPT interventions are based on social learning principles and aim to increase the frequency of adaptive child behaviors while reducing non-compliant or disruptive behavior. While they may provide additional benefit for reducing ADHD symptoms, they may also have positive effects on child and parental well-being beyond symptom reduction **(3)**.

These interventions involve teaching the parents specific skills to address their children's problematic behavior through programs such as Parent-Child Interaction Therapy (PCIT), group-based parent training Positive Parenting Program (Triple P). These interventions have been shown to improve child behavior and reduce ADHD symptoms in preschool-aged children. **(27)**

a- Parent-Child Interaction Therapy (PCIT)

This therapy is delivered to individual families by a therapist and consists of two phases: child-directed interaction and parent-directed interaction. The training is provided through a combination of didactic instruction, modeling, role-playing, and coaching. In PCIT, children attend most, but not all, of the sessions with their parents, and only the parents attend a single teaching session at the beginning of each phase. During the teaching sessions, which are attended only by the parents, they are taught all the skills for that phase. PCIT also emphasizes the role of traditional play therapy as part of their child-directed interaction phase. **(27)**

b- Group-based behavioral parent training (BPT)

It is a type of intervention for parents of children with ADHD and related disruptive behavioral disorders. It involves a manualized program that is delivered in a group format, typically over several weeks. The program focuses on teaching parents effective parenting strategies, such as positive attending, planned ignoring,

incentive systems, and time-out, to manage their child's behavior. The group format allows parents to learn from each other and provides social support. **(28)**

c- Triple P

A unique parent training program developed by Sanders, it is a multilevel parent training program that targets children aged 2–12 years old.

The program has five levels: **Level 1:** being a universal parent information strategy that makes general parenting information available to all parents by various strategies. **Level 2:** consists of a brief one or two-session primary healthcare-based parenting intervention targeting children with mild behavior problems. **Level 3:** is a four-session, more intensive parenting intervention that targets children with mild to moderate behavior problems. **Level 4:** is an 8–10 session individual or group parent training program targeting children with more significant behavior problems. **Level 5:** is an enhanced behavioral family intervention program that is utilized for significant behavior problems that are complicated by other factors (e.g., marital conflict, high stress). **(27)**

During treatment planning for parenting interventions, it is important for clinicians to consider factors that may lead to poorer treatment outcomes. These factors include broad co-morbidity in children, parental ADHD symptoms, parenting efficacy, and parental depressive symptoms. By taking these factors into account, clinicians can tailor interventions to address specific needs and improve treatment outcomes for children with ADHD. **(27)**

Classroom-based interventions

These interventions typically involve the use of behavioral strategies for teachers and the implementation of token economy or contingency-based programs to improve problematic classroom behavior. In addition to addressing behavioral issues, classroom-based interventions may also include components aimed at improving academic performance, such as shortening task length according to the child's attention span. It is important to ensure consistency in behavioral approach between home and school. Integration between home and school is vital in this regard. One effective way to promote communication between home and school is with daily report cards. These cards encourage parental reinforcement at home for behavior observed during the school day and can help to improve outcomes for children with ADHD **(29)**

II. Cognitive Behavior Therapy (CBT)

Regarding the use of psychotherapy interventions, cognitive-behavioral therapy (CBT) is a type of psychotherapy that aims to change a child's thought patterns. However, despite its potential benefits, randomized trials and systematic reviews have not found psychotherapy interventions to be effective in treating the core symptoms of ADHD in children. Nonetheless, CBT interventions have been shown to be helpful in managing coexisting conditions such as depression, anxiety, and social deficits. **(30)**

CBT may be a helpful adjunct to medications for adolescents with ADHD. It has the potential to improve organizational and planning skills, cognitive function, and coexisting psychiatric problems in this population. **(30)**

COGNITIVE TRAINING INTERVENTIONS

Neurofeedback (NF)

Regarding neurofeedback (NF) as a treatment approach for medical disorders, it is an extension of the biofeedback concepts, strategies, and techniques. NF, formerly known as electroencephalographic biofeedback, is based on the same classical/operant conditioning mechanisms of learning that underlie biofeedback. The use of NF as a treatment approach for ADHD aims to improve self-regulation of brain activity, typically measured through the electroencephalogram (EEG), using a brain-computer interface. NF has gained popularity due to its potential for lasting effects and longer clinical benefit after completion of treatment, as it may rely on procedural learning. **(31)**

b) PSYCHOEDUCATION

It is worth noting that psychoeducation has been recommended by various international clinical guidelines, including, the National Institute for Health and Care Excellence, and Psychoeducation programs for ADHD aim to provide general information about the disorder through various means such as presentations, videotapes, handouts, and group discussions. The information typically includes a description of ADHD and its symptoms, education about the epidemiology and etiology of ADHD, statistics on frequently co-occurring disorders such as conduct disorder and learning disorders, information about the life span prognosis for individuals with ADHD, and education about the pros and cons of the different available treatment approaches. These programs may be useful for helping individuals with ADHD and their families to better understand the disorder and to make informed decisions about treatment options. (32).

complementary and alternative methods

DIET

Meta-analyses have shown that restricted food coloring diets and omega-3 supplementation can be effective in reducing ADHD symptoms. However, it is important to note that the effect sizes are small and study inclusion is often restricted to families where parents have reported an adverse link between food and their child's behavior. Therefore, when parents report a link between food and drink consumption and their child's behavior, they should be encouraged to keep a food diary, and clinicians should consider referring them to a dietician if necessary (32).

Devices

a) External trigeminal nerve stimulation (eTNS)

It has been reported that there are two devices that have received FDA approval for the treatment of ADHD: Monarch eTNS System and EndeavorRx.

Monarch eTNS System is the first device-based ADHD treatment that has received clearance from the FDA. TNS is a noninvasive neuromodulation technique based on the hypothesis that electrical stimulation of the trigeminal nerve (supraorbital branch) affects the areas of the brain thought to be involved in ADHD. These areas are the anterior cingulate, inferior frontal gyrus, medial and middle frontal gyri, which are known to be important in regulating executive functions that are impaired in patients with ADHD. It is currently being used as a monotherapy treatment in ADHD patients aged 7-12 years old under the supervision of a caregiver. (33)

b) EndeavorRx

Regarding EndeavorRx, also known as ProjectEVO AKL-T01, it is a game-based digital therapeutic device that is the first of its kind and has been approved by the FDA. This intervention is available by prescription for children aged 8 to 12 years with primarily the inattentive or combined presentation of ADHD and is intended to be used with other ADHD treatment modalities. The device was developed with the aim of engaging children using high-quality graphics and reward loops, while also providing feedback on progress and compliance. It is designed to target specific areas of the brain that are responsible for attention, which can lead to improvements in attention, inhibitory control, and working memory, all of which are commonly affected in patients with ADHD. As such, it can be concluded that devices such as EndeavorRx hold promise as a rapidly developing drug-free alternative for the treatment of ADHD. (33)

3) Combination therapy:

Combination therapy uses both psychosocial interventions and medications. It may be warranted in preschool children who do not respond to behavioral interventions alone. In a systematic review and a meta-analysis, combination therapy with medications and behavior/psychological therapy was superior to behavior/psychological therapy alone. Combination therapy may be beneficial for school-aged children and adolescents who have a suboptimal response to pharmacotherapy, have a coexisting condition, or experience stressors in family life. In systematic reviews of randomized trials (including the Multimodal Treatment Study of Children with ADHD), combined medication and behavior treatment was no more effective than medication

treatment alone in improving core symptoms of ADHD. However, children receiving combined treatment may require lower doses of medication and achieve greater improvement in non-ADHD symptoms (eg, oppositional/aggressive, internalizing, teacher-rated social skills, caregiver-child relations, and reading achievement) than children receiving medication alone **(34)**

Treatment of coexisting conditions:

Up to one-third of children with ADHD have one or more coexisting conditions, such as (learning disorders, oppositional defiant disorder, conduct disorder, anxiety disorder, mood disorders, tics, and sleep disorders). **(Horst & Hendren 2005)** It is crucial to treat these coexisting conditions concurrently with ADHD, as the treatment of coexisting conditions may influence the treatment for ADHD. **(21)** To manage the full spectrum of symptoms in children with ADHD and coexisting conditions, adjunctive behavioral, psychological, and pharmacologic interventions may be necessary. **(22)**

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