I. Aetna considers certain services medically necessary for the assessment of attention deficit hyperactivity disorder (ADHD):

- Complete psychiatric evaluation (adults)
- Electroencephalography (EEG) or neurological consult when the presence of focal signs or clinical findings are suggestive of a seizure disorder or a degenerative neurological condition
- Laboratory evaluation (complete blood count [CBC], liver function tests [LFT]) and a cardiac evaluation and screening incorporating an electrocardiogram (ECG) if indicated, prior to beginning stimulant medication therapy
- Measurement of blood lead level for individuals with risk factors
- Medical evaluation (complete medical history and physical examination)
- Parent/child interview, or if adult, patient interview which may include obtaining information about the individual’s daycare, school or work functioning utilizing the criteria listed in the DSM-5. May also include an evaluation of comorbid psychiatric disorders and review of the

Policy History

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individual’s family and social history.

- Thyroid hormone levels if individual exhibits clinical manifestations of hyperthyroidism (eg, modest acceleration of linear growth and epiphyseal maturation, weight loss or failure to gain weight, excessive retraction of the eyelids causing lid lag and stare, diffuse goiter, tachycardia and increased cardiac output, increased gastrointestinal motility, tremor, hyperreflexia)

Notes:

Neuropsychological testing is not considered medically necessary for the clinical evaluation of persons with uncomplicated cases of ADHD. Psychological testing is not considered medically necessary for evaluation of children with uncomplicated cases of ADHD. In addition, neuropsychological or psychological testing performed solely for educational reasons may be excluded from coverage, as many Aetna benefit plans exclude coverage of educational testing; please check benefit plan descriptions. Neuropsychological testing may be medically necessary in neurologically complicated cases of ADHD (e.g., post head trauma, seizures). (See CPB 0158 - Neuropsychological and Psychological Testing (../100_199/0158.html)).

Referral to an outpatient mental health or chemical dependency provider may be medically necessary for the evaluation and comprehensive bio-psychosocial treatment for these disorders in collaboration with primary care physicians and other specialists.

II. Aetna considers pharmacotherapy and behavioral modification medically necessary for treatment of ADHD*.

III. Aetna considers the following experimental and investigational for the assessment and treatment of ADHD because the peer-reviewed medical literature does not support the use of these procedures/services for this indication.

A. Assessment:
- Actometer/Actigraph (see CPB 710 - Actigraphy and Accelerometry (/700_799/0710.html))
- Computerized EEG (brain mapping or neurometrics (see CPB 0221 - Quantitative EEG (Brain Mapping) (/200_299/0221.html))
- Computerized tests of attention and vigilance (continuous performance tests) (eg, Gordon Diagnostic System)
- Education and achievement testing*
- EEG theta/beta power ratio for the diagnosis of attention deficit hyperactivity disorder
- Electronystagmography (in the absence of symptoms of vertigo or balance dysfunction)
- Evaluation of iron status (e.g., measurement of serum iron and ferritin levels)
- Event-related potentials (see CPB 0181 - Evoked Potential Studies (/100_199/0181.html))
- Functional near-infrared spectroscopy (fNIRS)
- Hair analysis (see CPB 0300 - Hair Analysis (/300_399/0300.html))
- IgG blood tests (for prescription of diet)
- Measurement of zinc
- Neuroimaging (e.g., CT, CAT, MRI [including diffusion tensor imaging], magnetic resonance spectroscopy (MRS), PET and SPECT)
- Neuropsychiatric EEG-based assessment aid (NEBA) System
- Otoacoustic emissions (in the absence of signs of hearing loss)
- Pharmacogenetic testing of drug response
- Quotient ADHD system/test
- SNAP25 gene polymorphisms testing
- Transcranial magnetic stimulation-evoked measures (e.g., short interval cortical inhibition in motor cortex) as a marker of ADHD symptoms
- Tympanometry (in the absence of hearing loss)

B. Treatment:

- Acupuncture
- Anti-candida albicans medication
- Anti-fungal medications
- Anti-motion-sickness medication
- Applied kinesiology
- Brain integration therapy
- Chelation
- Chiropractic manipulation
- Cognitive behavior modification (cognitive rehabilitation)
- Computerized training on working memory (e.g., Cogmed and RoboMemo)*
- Deep pressure sensory vest
- Dietary counseling and treatments (i.e., Feingold diet)
- Dore program/dyslexia-dyspraxia attention treatment (DDAT)
- Educational intervention (e.g., classroom environmental manipulation, academic skills training, and parental training)*
- EEG biofeedback, also known as neurofeedback (see CPB 0132 - Biofeedback (../100_199/0132.html))
- Herbal remedies (e.g., Bach flower)
- Homeopathy
- Intensive behavioral intervention programs (e.g., applied behavior analysis [ABA], early intensive behavior intervention [EIBI], intensive behavior intervention [IBI], and Lovaas therapy)
- Megavitamin therapy (see CPB 0388 - Complementary and Alternative Medicine (../300_399/0388.html))
- Metronome training (see CPB 0325 - Physical Therapy Services (../300_399/0325.html))
- Mineral supplementation (e.g., iron, magnesium and zinc)

Music therapy (see CPB 0388 - Complementary and Alternative Medicine (../300_399/0388.html))

Neurofeedback (EEG biofeedback)

Optometric vision training/Irlen lenses

Psychopharmaceuticals: lithium, benzodiazepines, and selective serotonin re-uptake inhibitors*

Reboxetine

Sensory (auditory) integration therapy (see CPB 0256 -
Sensory and Auditory Integration Therapy (../200_299/0256.html)

- The Good Vibrations device*
- The Neuro-Emotional Technique
- Therapeutic eurythmy (movement therapy)
- Transcranial magnetic stimulation/cranial electrical stimulation (see CPB 0469 - Transcranial Magnetic Stimulation and Cranial Electrical Stimulation (0469.html))
- Vayarin (phosphatidylserine-containing omega3 long-chain polyunsaturated fatty acids)
- Vision therapy
- Yoga (see CPB 0388 - Complementary and Alternative Medicine (../300_399/0388.html))

* Notes:

- Coverage of pharmacotherapies is subject to the member's specific benefits for drug coverage. Please check benefit plan descriptions for details.
- Many Aetna plans exclude coverage of educational interventions. Please check benefit plan descriptions for details.
- Psychotherapy is covered under Aetna mental health benefits if the member also exhibits anxiety and/or depression.

Background
Attention deficit/hyperactivity disorder (ADHD) is a common condition among children and adolescents, and has been diagnosed with increased frequency in adults. It is characterized by symptoms of inattention and/or hyperactivity/impulsivity that have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level. Usually, some symptoms that caused impairment were present before the age of 7 years. Some impairment from the symptoms is present in 2 or more settings (e.g., at home and at school). Other causes of symptoms (e.g., schizophrenia, psychotic disorder, mood disorder, anxiety disorder, or personality disorder) should be ruled out.
Attention deficit hyperactivity disorder (ADHD) is one of the most common neuro-behavioral disorders of childhood. Approximately eight to ten percent of school age children are diagnosed with ADHD, with males predominantly more affected than females. Often, individuals with ADHD are affected by comorbidities, which are other conditions that exist simultaneously with and independent of ADHD. Examples include, but may not be limited to, anxiety disorder, conduct disorder, depression, oppositional defiant disorder and learning disabilities. Although ADHD is usually diagnosed in childhood, it may last into adulthood.

The behavior of individuals with ADHD may generally be classified into three subtypes; predominantly inattentive, predominately hyperactive-impulsive or a combination of the two.

ADHD is characterized by a pattern of behavior, present in multiple settings (eg, school and home), that can result in performance issues in social, educational or work settings. There is no single test to diagnose ADHD. Typically, a diagnosis is made by a comprehensive exam that assesses the onset and course of symptoms consistent with ADHD. A functional assessment, if conducted, evaluates both the severity of impairment and the pervasiveness of symptoms occurring in different environments.

The parameters for diagnosing ADHD are found in the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), published by the American Psychiatric Association (APA). The DSM-5 includes a set of diagnostic criteria that indicate the symptoms that must be present to establish the diagnosis of ADHD.

There are several types of specialists qualified to diagnose and treat ADHD. Examples include, but may not be limited to, child psychiatrists, family physicians, pediatricians, psychiatrists or neurologists. The treatments for ADHD may involve pharmacotherapy and nonpharmacologic therapy, including such interventions as individual and/or family psychotherapy.

There is no specific test for ADHD; its diagnosis is a clinical one. A parent/child interview is the cornerstone in the assessment of
ADHD in children and adolescents. It is used to rule out other psychiatric or environmental causes of symptoms. A medical evaluation with a complete medical history and a physical examination is necessary.

According to the American Academy of Child and Adolescent Psychiatry (AACAP)’s Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder, neuropsychological testing of children for the purpose of diagnosing ADHD is not considered necessary, unless there is strong evidence of a possible neurological disorder. There are few medical conditions which present with ADHD-like symptoms and most patients with ADHD have unremarkable medical histories. Neuropsychological assessment may be useful in neurologically-complicated cases of ADHD; however, such testing does not confirm the diagnosis of ADHD.

In general, attention-deficit disorders are best diagnosed through a careful history and the use of structured clinical interviews and dimensionally-based rating scales. Most psychologists obtain behavior ratings at home from the parents and at school from the teacher. Examples of the rating scales commonly used by psychologists are the Achenbach Child Behavior Checklist, Conners Rating Scales, and ADHD Symptoms Rating Scale.

Measurement of blood level of lead is appropriate only if clinical or environmental risk factors are present. An electroencephalogram (EEG) provides a graphic record of the electrical activity of the brain. Electroencephalography or neurological consult is indicated only in the presence of focal signs or clinical suggestions of seizure disorder or degenerative condition.

Brain mapping is the computerized conversion of data from brain electrical potentials into colored topographical maps of the brain. Quantitative electroencephalograph (QEEG) involves digital technology and computerized EEG. There are insufficient data to support the usefulness of computerized EEG (brain mapping or neurometrics).
There are insufficient data to support event-related potentials, neuroimaging, computerized tests of attention and vigilance, or neuropsychological tests (e.g., Test of Variables of Attention, the Continuous Performance Task, the Wisconsin Card-Sorting Test, the matching Familiar figures Test, and the Wechsler Intelligence Scale for Children-Revised). However, neuropsychological testing may be required in neurologically complicated cases of ADHD (e.g., post head trauma, seizures). There are no data to support the use of hair analysis or measurement of zinc.

Medical management of ADHD entails the use of stimulants -- methylphenidate (Ritalin), dextroamphetamine (Dexedrine), methamphetamine (Desoxyn), as well as an amphetamine-dextroamphetamine combination (Adderall). Pemoline (Cylert) is restricted to secondary use because of hepatic dysfunction associated with its use. Tricyclic anti-depressants are used for patients who do not respond to stimulants listed above, or for those who develop significant depression or other side effects on stimulants, or for the treatment of ADHD symptoms in patients with tics or Tourette's disorder. Psychotherapy is appropriate patients also exhibit anxiety and/or depression.

In a Cochrane review on the use of amphetamine for ADHD in people with intellectual disabilities (ID), Thomson et al (2009a) concluded that there is very little evidence for the effectiveness of amphetamine for ADHD in people with ID. The use of amphetamine in this population is based on extrapolation of research in people without ID. The authors stated that more research into effectiveness and tolerability is urgently needed. Furthermore another Cochrane review discussed the use of risperidone for ADHD in people with ID (Thomson et al, 2009b). The authors concluded that there is no evidence from randomized controlled trials that risperidone is effective for the treatment of ADHD in people with ID. The use of risperidone in this population is based on open-label studies or extrapolation from research in people with autism and disruptive behavioral disorders; however these studies have not investigated people with ID separately so there are reservations regarding the applicability of these findings. Research into effectiveness and tolerability is urgently needed.
There is a lack of scientific evidence to support the use of megavitamin therapy, herbal remedies, cognitive behavior modification, anti-motion-sickness medication, anti-candida-albicans medication, psychopharmaceuticals such as lithium, benzodiazepines, and selective serotonin re-uptake inhibitors, biofeedback, sensory (auditory) integration therapy, optometric vision training/IRlen lenses, chiropractic manipulation, or dietary interventions for the treatment of ADHD.

Konofal et al (2008) studied the effects of iron supplementation on ADHD in children. A total of 23 non-anemic children (aged 5 to 8 years) with serum ferritin levels less than 30 ng/ml who met DSM-IV criteria for ADHD were randomized (3:1 ratio) to either oral iron (ferrous sulfate, 80 mg/day, n = 18) or placebo (n = 5) for 12 weeks. There was a progressive significant decrease in the ADHD Rating Scale after 12 weeks on iron (-11.0 +/- 13.9; p < 0.008), but not on placebo (3.0 +/- 5.7; p = 0.308). Improvement on Conners' Parent Rating Scale (p = 0.055) and Conners' Teacher Rating Scale (p = 0.076) with iron supplementation therapy failed to reach significance. The mean Clinical Global Impression-Severity significantly decreased at 12 weeks (p < 0.01) with iron, without change in the placebo group. The authors concluded that iron supplementation appeared to improve ADHD symptoms in children with low serum ferritin levels suggesting a need for future investigations with larger controlled trials.

The American Academy of Pediatrics (2000) has the following statements regarding the diagnosis and evaluation of patients with ADHD:

- Available evidence does not support routine screening of thyroid function as part of the effort to diagnose ADHD.
- Current data do not support the use of any available continuous performance tests in the diagnosis of ADHD.
- Current literature does not support the routine use of EEG in the diagnosis of ADHD.
- Neuroimaging studies should not be used as a screening or diagnostic tool for children with ADHD because they are associated with high rates of false-positives and false-negatives.
- Regular screening of children for high lead levels does not aid in the diagnosis of ADHD.

Continuous performance tests are computer-based tests designed to measure inattention and impulsivity.

Neuropsychological and psychological testing for purely educational reasons are not generally considered medically necessary. This testing is usually provided by school systems under applicable state and federal rules. Neuropsychological testing may be medically necessary in neurologically complicated cases of ADHD (e.g., post head trauma, seizures). Children with uncomplicated ADHD do not require neuropsychological or psychological testing.

Feifel (1996) stated that ADHD may affect up to 3% of the adult population. Attention deficit hyperactivity disorder is not an acquired disorder of adulthood. Adults who were never diagnosed as having ADHD in childhood may present with many of the symptoms of the disorder. Inattention and distractibility, impulsivity, as well as hyperactivity are the classic hallmarks of ADHD, but adult patients often lack the full symptom complex, especially hyperactivity. Mood-associated symptoms (e.g., low frustration tolerance, irritability) are often present. In this regard, adults with ADHD usually have a difficult time with activities that require passive waiting. Adults with ADHD can be evaluated and successfully treated. Since the diagnosis is a clinical one, a comprehensive interview is the most important diagnostic procedure. A complete psychiatric evaluation with particular attention to the core symptoms of ADHD is essential for assessing ADHD in adults. Childhood history is also extremely important (Wender, 1998).

Wender developed ADHD criteria, known as the Utah criteria, which reflect the distinct features of the disorder in adults (Wender, 1998). The diagnosis of ADHD in an adult requires a longstanding history of ADHD symptoms, dating back to at least age 7. In the absence of treatment, such symptoms should have been consistently present without remission. In addition, hyperactivity and poor concentration should be present in
adulthood, along with 2 of the 5 additional symptoms: affective lability; hot temper; inability to complete tasks and disorganization; stress intolerance; and impulsivity.

The same medications used for children with ADHD are effective in adult patients. In a randomized controlled study (n = 146), Spencer et al (2005) concluded that robust doses of methylphenidate (average of 1.1mg/kg body weight/day) are effective in the treatment of adult ADHD. This is in agreement with the findings from a meta-analysis (Faraone et al, 2004) that the degree of efficacy of methylphenidate in treating ADHD adults is similar to what has been reported from meta-analyses of the child and adolescent literature. However, it should be noted that there is limited information regarding the long-term use of stimulants in adults (Kooij et al, 2004).

Kates (2005) noted that pharmacotherapies for patients with adult ADHD include stimulants and antidepressants; and medication can benefit up to 60 % of patients. In a randomized controlled study (n = 162), Wilens et al (2005) concluded that bupropion XL is an effective and well-tolerated non-stimulant treatment for adult ADHD. Adler et al (2005) stated that the results of an interim analysis (97 weeks) of an ongoing, open-label study (n = 384) support the long-term safety, effectiveness, and tolerability of another non-stimulant, atomoxetine, for the treatment of adult ADHD.

In a meta-analysis on the use of EEG biofeedback for the treatment of ADHD, Monastra and colleagues (2005) critically examined the empirical evidence, applying the efficacy guidelines jointly established by the Association for Applied Psychophysiology and Biofeedback (AAPB) and the International Society for Neuronal Regulation (ISNR). On the basis of these scientific principles, EEG biofeedback was deemed to be "probably efficacious" for the treatment of ADHD. Although significant clinical improvement was reported in about 75 % of the patients in each of the published research studies, additional randomized, controlled group studies are needed in order to provide a better estimate of the percentage of patients with ADHD who will demonstrate such gains in clinical practice.
van As and colleagues (2010) stated that neurofeedback is a method of treatment that is being used increasingly in the Netherlands, particularly in psychological practices. Many psychiatric and somatic symptoms are currently being treated with the help of neurofeedback. In particular, neurofeedback is being used more and more to ADHD. Despite its growing popularity, neurofeedback is still a relatively unknown treatment method in psychiatric practices. These investigators examined the scientific evidence for treating ADHD with neurofeedback. They searched the literature for reports on controlled trials that investigated the effectiveness of neurofeedback on ADHD. A total of 6 controlled trials were located. The studies reported that neurofeedback had a positive effect on ADHD, but all the studies were marred by methodological shortcomings. The authors concluded that on the basis of currently available research results, no firm conclusion can be drawn about the effectiveness of treating ADHD by means of neurofeedback. In view of the fact that neurofeedback is being used more and more as a method of treatment, there is an urgent need for scientific research in this field to be well-planned and carefully executed.

Actigraphy is the process of measuring physical movement of an individual over time to assess the degree of motor activities. Jensen and Kelly (2004) examined the effects of yoga on the attention and behavior of boys with ADHD. Subjects were randomly assigned to a 20-session yoga group (n = 11) or a control group (cooperative activities; n = 8). They were assessed pre- and post-intervention on the Conners’ Parent and Teacher Rating Scales-Revised: Long (CPRS-R:L & CTRS-R:L), the Test of Variables of Attention (TOVA), and the Motion Logger Actigraph. Data were analyzed using 1-way repeated measures analysis of variance (ANOVA). Significant improvements from pre-test to post-test were found for the yoga, but not for the control group on 5 subscales of the Conners' Parents Rating Scales (CPRS): Oppositional, Global Index Emotional Lability, Global Index Total, Global Index Restless/Impulsive and ADHD Index. Significant improvements from pre-test to post-test were found for the control group, but not the yoga group on 3 CPRS subscales: Hyperactivity, Anxious/Shy, and Social Problems. Both groups improved significantly on CPRS Perfectionism, DSM-IV
Hyperactive/ Impulsive, and DSM-IV Total. For the yoga group, positive change from pre- to post-test on the Conners' Teacher Rating Scales (CTRS) was associated with the number of sessions attended on the DSM-IV Hyperactive-Impulsive subscale and with a trend on DSM-IV Inattentive subscale. Those in the yoga group who engaged in more home practice showed a significant improvement on TOVA Response Time Variability with a trend on the ADHD score, and greater improvements on the CTRS Global Emotional Lability subscale. Results from the Motion Logger Actigraph were inconclusive. The authors noted that although these data did not provide strong support for the use of yoga for ADHD, partly because the study was under-powered, they did suggest that yoga may have merit as a complementary treatment for boys with ADHD already stabilized on medication, particularly for its evening effect when medication effects are absent. They stated that yoga remains an investigational treatment, and this study supported further research into its possible uses for this population. The authors stated that these findings need to be replicated on larger groups with a more intensive supervised practice program.

Working memory (WM) capacity is one's ability to retain and manipulate information during a short period of time. This ability underlies complex reasoning and has generally been regarded as a fixed trait of the individual. Children/adolescents with ADHD represent one group of patients with a WM deficit, attributed to an impairment of the frontal lobe (Martinussen et al, 2005). Cogmed and RoboMemo WM training are software-based approaches designed for children and adolescents with ADHD to improve their ability to concentrate and use problem solving skills after training.

Klingberg and colleagues (2005) conducted a multi-center, randomized, controlled, double-blind study to examine the effect of improving WM by computerized, systematic practice of WM tasks. A total of 53 children with ADHD (9 girls, 44 boys; 15 of 53 inattentive subtype), aged 7 to 12 years, without stimulant medication were included in the study. The compliance criterion (greater than 20 days of training) was met by 44 subjects, 42 of whom were also evaluated at follow-up 3 months later.
Participants were randomly assigned to use either the treatment computer program for training WM or a comparison program. The main outcome measure was the span-board task, a visuo-spatial WM task that was not part of the training program. For the span-board task, there was a significant treatment effect both post-intervention and at follow-up. In addition, there were significant effects for secondary outcome tasks measuring verbal WM, response inhibition, and complex reasoning. Parent ratings also showed significant reduction in symptoms of hyperactivity/impulsivity, and inattention, both post-intervention and at follow-up. The authors concluded that the findings of this study show that WM can be improved by training in children with ADHD. This training also improved response inhibition and reasoning and resulted in a reduction of the parent-rated inattentive symptoms of ADHD.

It is interesting to note that improvements with WM training lasted for 3 months following treatment. However, how long these improvements might persist is unclear. Furthermore, whether continued training is needed to maintain these gains over a longer duration has yet to be ascertained. Additionally, this study had several drawbacks: (i) only 9 of 53 subjects in this small study were girls, so that a larger study with more girls is needed to better assess overall efficacy and applicability of this therapy to girls with ADHD; (ii) because individuals with depression and/or co-occurring oppositional defiant disorder were excluded, the extent to which these findings could be extrapolated to children/adolescents with ADHD and these behavioral conditions is unknown. Since many children/adolescents with ADHD also have these conditions, it will be important to determine if WM training is beneficial to these children/adolescents as well; (iii) the absence of teacher-reported improvements is of particular concern. Although these investigators suggested that parental ratings are more reliable because they were consistent with the executive functioning results, the basis for this suggestion is unclear. Since an objective of ADHD therapy is to improve patients' functioning at school, demonstrating that WM training achieves this goal is important.

Preliminary data suggested that computerized training of WM
may be an effective treatment for children/adolescents with ADHD. However, more research is needed to establish the effectiveness of this approach.

Rickson (2006) compared the impact of instructional and improvisational music therapy approaches on the level of motor impulsivity displayed by adolescent boys (n = 13) who have ADHD. A combination of a multiple contrasting treatment and an experimental control group design was used. No statistical difference was found between the impact of the contrasting approaches as measured by a Synchronized Tapping Task (STT) and the parent and teacher versions of Conners’ Rating Scales Restless-Impulsive (R-I) and Hyperactive-Impulsive (H-I) subscales. The author noted that while no firm conclusions can be drawn, there are indications that the instructional approach may have contributed to a reduction of impulsive and restless behaviors in the classroom. In addition, over the period of the study, both music therapy treatment groups significantly improved accuracy on the STT, and teachers reported a significant reduction in Conners’ DSM-IV Total and Global Index subscale scores. The author concluded that these findings tentatively suggested that music therapy may contribute to a reduction in a range of ADHD symptoms in the classroom, and that increasing accuracy on the STT could be related to improvement in a range of developmental areas—not specifically motor impulsivity.

Altunc et al (2007) evaluated the evidence of any type of therapeutic or preventive intervention testing homeopathy for childhood and adolescence ailments. Systematic literature searches were conducted in MEDLINE, EMBASE, AMED, CINAHL, Cochrane Central, British Homeopathic Library, ClinicalTrials.gov, and the UK National Research Register. Bibliographies were checked for further relevant publications. Studies were selected according to pre-defined inclusion and exclusion criteria. All double-blind, placebo-controlled randomized clinical trials of any homeopathic intervention for preventing or treating childhood and adolescence ailments were included. According to the classification of the World Health Organization, the age range defined for inclusion was 0 to 19 years. Study selection, data extraction, and assessment of methodological quality were
performed independently by 2 reviewers. A total of 326 articles were identified, 91 of which were retrieved for detailed evaluation. Sixteen trials that assessed 9 different conditions were included in the study. With the exception of ADHD and acute childhood diarrhea (each tested in 3 trials), no condition was evaluated in more than 2 double-blind randomized clinical trials. The evidence for ADHD and acute childhood diarrhea is mixed, showing both positive and negative results for their respective main outcome measures. For adenoid vegetation, asthma, and upper respiratory tract infection each, 2 trials are available that suggest no difference compared with placebo. For 4 conditions, only single trials are available. The authors concluded that the evidence from rigorous clinical trials of any type of therapeutic or preventive intervention testing homeopathy for childhood and adolescence ailments is not convincing enough for recommendations in any condition.

The Good Vibrations device is a radio-frequency instrument whose main objective is to teach children to pay better attention in class. It supposedly achieves this goal through the sending and receiving of gentle, pager-like vibrations from teacher to student. This device consists of 2 units: (i) a sending unit (teacher unit), and (ii) a receiving unit (student unit -- wristwatch). The teacher can send 2 types of vibrational signals -- one when the toggle switch is pressed down, triggering a long vibration (the reminder vibration) and the other when the button is pressed up, which triggers 4 short vibrations (the positive vibration. There is a lack of evidence regarding he effectiveness of this device in treating children with ADHD.

Karpouzis et al (2009) stated that the Neuro-Emotional Technique (NET), a branch of chiropractic, was designed to address the biopsychosocial aspects of acute and chronic conditions including non-musculoskeletal conditions. Anecdotally, it has been suggested that ADHD may be managed effectively by NET. A placebo-controlled, double-blind, randomized clinical trial was designed to assess the effectiveness of NET on a cohort of children with medically diagnosed ADHD. Children aged 5 to 12 years who met the inclusion criteria were randomixed to one of 3 groups -- the control group continued on their existing medical
regimen and the intervention and placebo groups had the addition of the NET and sham NET protocols added to their regimen respectively. These 2 groups attended a clinical facility twice-weekly for the first month and then once-monthly for 6 months. The Conners' Parent and Teacher Rating Scales (CRS) were used at the start of the study to establish baseline data and then in 1 month and in 7 months time, at the conclusion of the study. The primary outcome measures chosen were the Conners' ADHD Index and Conners' Global Index. The secondary outcome measures chosen were the DSM-IV: Inattentive, the DSM-IV: Hyperactive-Impulsive, and the DSM-IV: Total subscales from the Conners' Rating Scales, monitoring changes in inattention, hyperactivity and impulsivity. Calculations for the sample size were set with a significance level of 0.05 and the power of 80%, yielding a sample size of 93. The authors concluded that the present study should provide information as to whether the addition of NET to an existing medical regimen can improve outcomes for children with ADHD.

Neale and colleagues (2010) noted that although twin and family studies have shown ADHD to be highly heritable, genetic variants influencing the trait at a genome-wide significant level have yet to be identified. As prior genome-wide association studies (GWAS) have not yielded significant results, these researchers conducted a meta-analysis of existing studies to boost statistical power. They used data from 4 projects: (i) the Children's Hospital of Philadelphia (CHOP); (ii) phase I of the International Multicenter ADHD Genetics project (IMAGE); (iii) phase II of IMAGE (IMAGE II); and (iv) the Pfizer-funded study from the University of California, Los Angeles, Washington University, and Massachusetts General Hospital (PUWMA). The final sample size consisted of 2,064 trios, 896 cases, and 2,455 controls. For each study, these investigators imputed HapMap single nucleotide polymorphisms, computed association test statistics and transformed them to z-scores, and then combined weighted z-scores in a meta-analysis. No genome-wide significant associations were found, although an analysis of candidate genes suggests that they may be involved in the disorder. The authors concluded that given that ADHD is a highly heritable disorder, these negative results suggested that the effects of common
ADHD risk variants must, individually, be very small or that other types of variants, e.g., rare ones, account for much of the disorder's heritability.

The Quotient ADHD System consists of an infrared motional tracking system (similar to a computer kiosk) that includes a head reflector (used for individuals of all ages) and a leg reflector (used for individuals older than age 13) to measure motion, attention and attention state. Integrated composite scores of 19 indices purport to indicate the level and severity of inattention, hyperactivity and impulsivity compared with individuals of the same age and gender. The Quotient ADHD system/test takes 15 mins for children under the age of 13 years, or 20 mins for adolescents and adults. The system collects data on the person’s ability to sit still, inhibit impulsivity and respond accurately to images on a computer screen. The report provides analysis of motion, attention and shifts in attention states. Integrated composite scores report the level and severity of inattention, hyperactivity and impulsivity compared to other people of the same age and gender. The data are uploaded via a secure internet portal and the report is available within minutes. The clinician integrates the Quotient ADHD test report with information from other assessment tools and the clinical evaluation to help guide the discussion on treatment plan. There is a lack of scientific evidence regarding the validity of the Quotient ADHD test as a management tool for ADHD.

In a case-control study, Gilbert et al (2011) examined if transcranial magnetic stimulation (TMS)-evoked measures, particularly short interval cortical inhibition (SICI), in motor cortex correlate with the presence and severity of ADHD in childhood as well as with commonly observed delays in motor control. Behavioral ratings, motor skills, and motor cortex physiology were evaluated in 49 children with ADHD (mean age of 10.6 years, 30 boys) and 49 typically developing children (mean age of 10.5 years, 30 boys), all right-handed, aged 8 to 12 years. Motor skills were evaluated with the Physical and Neurological Examination for Subtle Signs (PANESS) and the Motor Assessment Battery for Children version 2; SICI and other physiologic measures were obtained using TMS in the left motor cortex. In children with
ADHD, mean SICI was reduced by 40 % (p < 0.0001) and less SICI correlated with higher ADHD severity (r = -0.52; p = 0.002). Mean PANESS motor development scores were 59 % worse in children with ADHD (p < 0.0001). Worse PANESS scores correlated modestly with less SICI (r = -0.30; p = 0.01). The authors concluded that reduced TMS-evoked SICI correlates with ADHD diagnosis and symptom severity and also reflects motor skill development in children. They noted that "[t]his study was cross-sectional, and a longitudinal study might provide more readily interpretable insights into the relationship between age-related motor development, motor physiology, and ADHD...Such studies in ADHD in children might further enhance our understanding of SICI as a quantitative, biologically based marker of ADHD symptoms".

In a randomized controlled trial (the INCA Trial), Pelsser et al (2011) examined if there is a connection between diet and behavior in an unselected group of children. The "Impact of Nutrition on Children with ADHD (INCA)" study consisted of an open-label phase with masked measurements followed by a double-blind cross-over phase. Patients in the Netherlands and Belgium were enrolled via announcements in medical health centers and through media announcements. Randomization in both phases was individually done by random sampling. In the open-label phase (1st phase), children aged 4 to 8 years who were diagnosed with ADHD were randomly assigned to 5 weeks of a restricted elimination diet (diet group) or to instructions for a healthy diet (control group). Thereafter, the clinical responders (those with an improvement of at least 40 % on the ADHD rating scale [ARS]) from the diet group proceeded with a 4-week double-blind cross-over food challenge phase (2nd phase), in which high-IgG or low-IgG foods (classified on the basis of every child's individual IgG blood test results) were added to the diet. During the 1st phase, only the assessing pediatrician was masked to group allocation. During the 2nd phase (challenge phase), all persons involved were masked to challenge allocation. Primary end points were the change in ARS score between baseline and the end of the 1st phase (masked pediatrician) and between the end of the 1st phase and the 2nd phase (double-blind), and the abbreviated Conners' scale (ACS) score (unmasked) between the
same time points. Secondary end points included food-specific IgG levels at baseline related to the behavior of the diet group responders after IgG-based food challenges. The primary analyses were intention-to-treat for the 1st phase and per protocol for the 2nd phase. Between November 4, 2008 and September 29, 2009, a total of 100 children were enrolled and randomly assigned to the control group (n = 50) or the diet group (n = 50). Between baseline and the end of the 1st phase, the difference between the diet group and the control group in the mean ARS total score was 23.7 (95 % confidence interval [CI]: 18.6 to 28.8; p < 0.0001) according to the masked ratings. The difference between groups in the mean ACS score between the same time points was 11.8 (95 % CI: 9.2 to 14.5; p < 0.0001). The ARS total score increased in clinical responders after the challenge by 20.8 (95 % CI: 14.3 to 27.3; p < 0.0001) and the ACS score increased by 11.6 (7.7 to 15.4; p < 0.0001). In the challenge phase, after challenges with either high-IgG or low-IgG foods, relapse of ADHD symptoms occurred in 19 of 30 (63 %) children, independent of the IgG blood levels. There were no harms or adverse events reported in both phases. The authors concluded that a strictly supervised restricted elimination diet is a valuable instrument to assess whether ADHD is induced by food. Moreover, the prescription of diets on the basis of IgG blood tests should be discouraged.

van Ewijk and colleagues (2012) stated that diffusion tensor imaging (DTI) allows in-vivo examination of the microstructural integrity of white matter brain tissue. These researchers performed a systematic review and quantitative meta-analysis using GingerALE to compare current DTI findings in patients with ADHD and healthy controls to further unravel the neurobiological underpinnings of the disorder. Online databases were searched for DTI studies comparing white matter integrity between ADHD patients and healthy controls. A total of 15 studies met inclusion criteria. Alterations in white matter integrity were found in widespread areas, most consistently so in the right anterior corona radiata, right forceps minor, bilateral internal capsule, and left cerebellum, areas previously implicated in the pathophysiology of the disorder. The authors concluded that while more research is needed, DTI proves to be a promising
technique, providing new prospects and challenges for future research into the pathophysiology of ADHD.

VandenBerg (2001) noted that children described as having attention deficit hyperactivity disorder often demonstrate inability to sustain visual attention during classroom fine motor activities. This study investigated the effect of wearing a weighted vest (deep-pressure sensory input) on children's on-task behavior in the classroom. A total of 4 students with documented attention difficulties and hyperactivity were timed with a stop-watch to measure their on-task behavior during fine motor activities in the classroom. All 4 students were timed for 6 15-min observations without wearing a weighted vest and for 6 15-min observations while wearing a weighted vest. On-task behavior increased by 18 % to 25 % in all 4 students while they were wearing the weighted vest. Additionally, 3 of the 4 students frequently asked to wear the vest other than during the observation times. The authors concluded that these preliminary findings supported the hypothesis that wearing a weighted vest to apply deep pressure increases on-task behavior during fine motor activities. These preliminary findings need to be validated by well-designed studies.

The Dore program (also known dyslexia-dyspraxia attention treatment [DDAT]) is a drug-free, exercise-based program that is employed for the treatment of patients with ADHD, Asperger’s syndrome, dyslexia, dyspraxia, and other learning difficulties. It consists of a specialized neurological evaluation and series of patient-specific exercises designed to improve the functioning of the cerebellum, based on Dore's belief that the cerebellum facilitates skill development and thus plays an essential role in the learning process. The theory is that the size and function of the cerebellum are related to a group of learning disorders referred to as cerebellar developmental delay (CDD). Currently, there is insufficient evidence to support the effectiveness of the Dore program for the treatment of patients with ADHD.

In a review on “Curing dyslexia and attention-deficit hyperactivity disorder by training motor co-ordination”, Bishop (2007) noted that “the published studies are seriously flawed. On measures
where control data are available, there is no credible evidence of significant gains in literacy associated with this intervention. There are no published studies on efficacy with the clinical groups for whom the programme is advocated”. The author stated that the publication of 20 papers in peer-reviewed scientific journal (Dyslexia) has been presented as giving further credibility to the treatment. However, the research community in this area has been dismayed that work of such poor standard has been published. Bishop also noted that the research purporting to show effectiveness of the treatment does not show sustained gains in literacy scores in treated versus control children. Furthermore, the intervention has not been evaluated on the clinical groups for which it is recommended.

Furthermore, Rack et al (2007) stated that Reynolds and Nicolson (Dyslexia: An International Journal of Research & Practice, 2007) reported follow-up data 12 and 18 months after a period of intervention consisting of an exercise-based treatment program (DDAT). The findings suggested the treatment had effects on bead threading, balance, rapid naming, semantic fluency and working memory but not on reading or spelling. These investigators argued that the design of the study was flawed, the statistics used to analyze the data were inappropriate, and reiterated other issues raised by them and others in 2003. The authors concluded that current evidence provided no support for the claim that DDAT is effective in improving children’s literacy skills.

A metronome is a mechanical or electrical instrument that makes repeated clicking sounds at an adjustable pace, used for marking rhythm. With interactive metronome therapy, a computerized metronome produces a rhythmic beat that patients attempt to match with hand or foot tapping. It is theorized that matching the beat over repeated sessions will reflect gains in motor planning and timing skills. In a case-report, Bartscherer and Dole (2005) described a new intervention, the Interactive Metronome (Sunrise, FL), for improving timing and coordination. A 9-year old boy, with difficulties in attention and developmental delay of unspecified origin underwent a 7-week training program with the Interactive Metronome. Before, during, and after training timing,
accuracy was assessed with testing procedures consistent with the Interactive Metronome training protocol. Before and after training, his gross and fine motor skills were examined with the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP). The child exhibited marked change in scores on both timing accuracy and several BOTMP subtests. Additionally his mother relayed anecdotal reports of changes in behavior at home. This child's participation in a new intervention for improving timing and coordination was associated with changes in timing accuracy, gross and fine motor abilities, and parent reported behaviors. The authors stated that these findings warrant further study.

Cosper et al (2009) examined the effectiveness of Interactive Metronome training in a group of children with mixed attentional and motor coordination disorders to further explore which subcomponents of attentional control and motor functioning the training influences. A total of 12 children who had been diagnosed with ADHD, in conjunction with either developmental coordination disorder (n = 10) or pervasive developmental disorder (n = 2), underwent 15 1-hour sessions of Interactive Metronome training over a 15-week period. Each child was assessed before and after the treatment using measures of attention, coordination, and motor control to determine the effectiveness of training on these cognitive and behavioral realms. As a group, the children made significant improvements in complex visual choice reaction time and visuo-motor control after the training. There were, however, no significant changes in sustained attention or inhibitory control over inappropriate motor responses after treatment. The authors concluded that these findings suggested Interactive Metronome training may address deficits in visuo-motor control and speed, but appears to have little effect on sustained attention or motor inhibition.

An Institute for Clinical Systems Improvement’s clinical practice guideline on “Diagnosis and management of attention deficit hyperactivity disorder in primary care for school-age children and adolescents” (Dobie et al, 2012) as well as an UpToDate review on “Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis” (Krull, 2013) do not mention the use of Dore program/dyslexia-dyspraxia
attention treatment (DDAT), intensive behavioral intervention programs (e.g., applied behavior analysis [ABA], early intensive behavior intervention [EIBI], intensive behavior intervention [IBI], and Lovaas therapy), and metronome training as treatment modalities.

On July 15, 2013, the Food and Drug Administration (FDA) allowed marketing of the first medical device (Neuropsychiatric EEG-Based Assessment Aid (NEBA) System, NEBA Health of Augusta, GA), based on brain function to help assess ADHD in children and adolescents 6 to 17 years old. When used as part of a complete medical and psychological examination, the device can help confirm an ADHD diagnosis or a clinician’s decision that further diagnostic testing should focus on ADHD or other medical or behavioral conditions that produce symptoms similar to ADHD. The NEBA System is based on EEG technology, which records different kinds of brain waves given off by neurons and their frequency. The NEBA System is a 15- to 20-min non-invasive test that calculates the ratio of 2 standard brain wave frequencies, known as theta and beta waves. The theta/beta ratio has been shown to be higher in children and adolescents with ADHD than in children without it. The FDA reviewed the NEBA System through the de-novo classification process, a regulatory pathway for some low- to moderate-risk medical devices that are not substantially equivalent to an already legally marketed device. However, there is currently insufficient evidence that the NEBA system is effective in the diagnosis of ADHD.

Lansbergen et al (2011) stated that ADHD was found to be characterized by a deviant pattern of electro-cortical activity during resting state, particularly increased theta and decreased beta activity. The first objective of the present study was to confirm whether individuals with slow alpha peak frequency contribute to the finding of increased theta activity in ADHD. The second objective was to explore the relation between resting-state brain oscillations and specific cognitive functions. From 49 boys with ADHD and 49 healthy control boys, resting-state EEG during eyes open and eyes closed was recorded, and a variety of cognitive tasks were administered. Theta and beta power and
theta/beta ratio were calculated using both fixed frequency bands and individualized frequency bands. As expected, theta/beta ratio, calculated using fixed frequency bands, was significantly higher in ADHD children than control children. However, this group effect was not significant when theta/beta ratio was assessed using individualized frequency bands. No consistent relation was found between resting-state brain oscillations and cognition. The present results suggested that previous findings of increased theta/beta ratio in ADHD may reflect individuals with slow alpha peak frequencies in addition to individuals with true increased theta activity. Therefore, the often reported theta/beta ratio in ADHD can be considered a non-specific measure combining several distinct neurophysiological subgroups such as frontal theta and slowed alpha peak frequencies. The authors concluded that future research should elucidate the functional role of resting-state brain oscillations by investigating neurophysiological subgroups, which may have a clearer relation to cognitive functions than single frequency bands.

Loo and Makeig (2012) noted that psychiatric research applications of EEG, the earliest approach to imaging human cortical brain activity, are attracting increasing scientific and clinical interest. For more than 40 years, EEG research has attempted to characterize and quantify the neurophysiology of ADHD, most consistently associating it with increased fronto-central theta band activity and increased theta to beta (θ/β) power ratio during rest compared to non-ADHD controls. Recent reports suggested that while these EEG measures demonstrate strong discriminant validity for ADHD, significant EEG heterogeneity also exists across ADHD-diagnosed individuals. In particular, additional studies validating the use of the θ/β power ratio measure appear to be needed before it can be used for clinical diagnosis. In recent years, the number and the scientific quality of research reports on EEG-based neuro-feedback (NF) for ADHD have grown considerably, although the studies reviewed here do not yet support NF training as a first-line, stand-alone treatment modality. In particular, more research is needed comparing NF to placebo control and other effective treatments for ADHD. Currently, after a long period of relative stasis, the
neurophysiological specificity of measures used in EEG research is rapidly increasing. It is likely, therefore, that new EEG studies of ADHD using higher density recordings and new measures drawn from viewing EEG as a 3-dimensional functional imaging modality, as well as intensive re-analyses of existing EEG study data, can better characterize the neurophysiological differences between and within ADHD and non-ADHD subjects, and lead to more precise diagnostic measures and effective NF approaches.

Liechti et al (2013) stated that the resting EEG reflects development and arousal, but whether it can support clinical diagnosis of ADHD remains controversial. These investigators examined if the theta power and theta/beta ratio is consistently elevated in ADHD and younger age as proposed. Topographic 48-channel EEG from 32 children (8 to 16 years) and 22 adults (32 to 55 years) with ADHD and matched healthy controls (n = 30 children/21 adults) was compared. Following advanced artefact correction, resting EEG was tested for increased theta and theta/beta activity due to ADHD and due to normal immaturity. Discriminant analyses tested classification performance by ADHD and age using these EEG markers as well as EEG artefacts and deviant attentional event-related potentials (ERPs). No consistent theta or theta/beta increases were found with ADHD. Even multivariate analyses indicated only marginal EEG power increases in children with ADHD. Instead, consistent developmental theta decreases were observed, indicating that maturational lags of fewer than 3 years would have been detected in children. Discriminant analysis based on proposed simple spectral resting EEG markers was successful for age but not for ADHD (81 versus 53 % accuracy). Including ERP markers and EEG artefacts improved discrimination, although not to diagnostically useful levels. The authors concluded that the lack of consistent spectral resting EEG abnormalities in ADHD despite consistent developmental effects casts doubt upon conventional neurometric approaches towards EEG-based ADHD diagnosis, but is consistent with evidence that ADHD is a heterogeneous disorder, where the resting state is not consistently characterized by maturational lag.

Clarke et al (2013) noted that past research has reported that a
small proportion of children with ADHD have excess beta activity in their EEG, rather than the excess theta typical of the syndrome. This atypical group has been tentatively labeled as hyper-aroused. The aim of this study was to determine whether these children have a hyper-aroused central nervous system. Participants included 104 boys aged 8- to 13-year old, with a diagnosis of either the combined or inattentive type of ADHD (67 combined type), and 67 age-matched male controls. Ten and a half minutes of EEG and skin conductance (SCL) were simultaneously recorded during an eyes-closed resting condition. The EEG was Fourier transformed and estimates of total power, and relative power in the delta, theta, alpha, and beta bands, and the theta/beta ratio, were calculated. ADHD patients were divided into an excess beta group and a typical excess theta group. Relative to controls, the typical excess theta group had significantly increased frontal total power, theta and theta/beta ratio, with reduced alpha and beta across the scalp. The excess beta group had significantly reduced posterior total power, increased central-posterior delta, globally reduced alpha, globally increased beta activity, and globally reduced theta/beta ratio. Both ADHD groups had significantly reduced SCL compared to the control group, but the 2 groups did not differ from each other on SCL. These results indicated that ADHD children with excess beta activity are not hyper-aroused, and confirmed that the theta/beta ratio is not associated with arousal.

Dupuy et al (2013) examined sex differences between the EEGs of combined and inattentive types of ADHD within boys and girls aged 8 to 12 years. Subject groups included 80 ADHD combined type (40 boys and 40 girls), 80 ADHD inattentive type (40 boys and 40 girls) and 80 controls (40 boys and 40 girls). An eyes-closed resting EEG was recorded and Fourier transformed to provide estimates for absolute and relative power in the delta, theta, alpha and beta frequency bands, as well as total power and the theta/beta ratio. The boy ADHD groups, compared with boy controls, had greater absolute and relative theta, greater theta/beta ratio, reduced absolute and relative alpha, and reduced absolute and relative beta. The girl ADHD groups, compared with girl controls, had greater absolute delta, greater absolute and relative theta, greater theta/beta ratio, greater total
power, and reduced relative delta and relative beta. Between ADHD types, combined type boys had globally greater absolute and relative theta, greater theta/beta ratio, and less relative alpha than inattentive type boys. While topographical differences emerged, there were no significant global differences between ADHD types in girls. That is, EEG differences between ADHD types are dissimilar in boys and girls. Different EEG maturational patterns between boys and girls also obscure ADHD-related EEG abnormalities. The authors concluded that these results have important implications for the understanding of ADHD in girls. Ignoring such sex differences may have compromised the value of previous ADHD investigations, and these sex differences should be recognized in future research.

An UpToDate review on “Attention deficit hyperactivity disorder in children and adolescents: Clinical features and evaluation” (Krull, 2014) states that “The evaluation for ADHD does not require blood lead levels, thyroid hormone levels, neuroimaging, or electroencephalography unless these tests are indicated by findings in the clinical evaluation. Ancillary evaluation -- Other evaluations are not routinely indicated to establish the diagnosis of ADHD, but may be warranted to evaluate conditions remaining in the differential diagnosis after the initial assessment. These evaluations may include neurology consultation or electroencephalography (neurologic or seizure disorder)”.

An UpToDate review on “Clinical and laboratory diagnosis of seizures in infants and children” (Wilfong, 2014) states that “An EEG is recommended in the evaluation of a child with suspected seizures or epilepsy. In addition to providing support for the diagnosis of epilepsy, the EEG also helps define the epilepsy syndrome and directs optimal therapy. Obtaining a tracing in the awake and sleep states, in close proximity to an event, and repeating the tracing can increase the diagnostic yield of the study. Nonetheless, the sensitivity and specificity of EEG is imperfect”.

Wiley and Riccio (2014) examined the current state of research using functional near-infrared spectroscopy (fNIRS) imaging methods to evaluate neurological activation patterns of ADHD
populations. Informal search procedures were used to identify potential articles. Searches were conducted using EBSCO Academic Search Complete, ProQuest, and PsycINFO between March 1, 2014 and March 31, 2014. Search terms used were "near-infrared spectroscopy", "NIRS" and "fNIRS". To be included in the review, studies must have utilized an empirical design, collected data using fNIRS imaging methods, and have a specifically identified ADHD sample. A total of 10 studies were identified that met the inclusion criteria. Results were evaluated for recurrent themes and patterns of activation detected by fNIRS. Samples of ADHD displayed a consistent trend of altered activation patterns. Specifically, ADHD samples exhibited decreased levels of oxygenated hemoglobin levels during tasks. A similar pattern emerged for deoxygenated hemoglobin levels, but group differences were smaller. Results from studies investigating the effects of methylphenidate stimulant medications indicated that these altered activation patterns showed a normalization trend when participants began taking methylphenidate medications. The authors concluded that although fNIRS has been identified as a viable imaging technique with both temporal and spatial resolution, few studies have been conducted using fNIRS to evaluate neurological activation patterns in participants with ADHD. The clinical value of fNIRS has yet to be established by well-designed studies.

Furthermore, an UpToDate review on “Adult attention deficit hyperactivity disorder in adults: Epidemiology, pathogenesis, clinical features, course, assessment, and diagnosis” (Bukstein, 2015) does not mention functional near-infrared spectroscopy as a management tool.

Maneeton et al (2014) summarized the effectiveness, acceptability, and tolerability of bupropion in comparison with methylphenidate for ADHD treatment. Included studies were randomized controlled trials (RCTs) that compared bupropion and methylphenidate. Clinical studies conducted between January 1991 and January 2014 were reviewed. MEDLINE, EMBASE, CINAHL, PsycINFO, and the Cochrane Controlled Trials Register were searched in January 2014. Additionally, clinical trials were identified from the databases of ClinicalTrials.gov and the EU
Clinical Trials Register. All RCTs of bupropion and methylphenidate reporting final outcomes relevant to (i) ADHD severity, (ii) response or remission rates, (iii) overall discontinuation rate, or (iv) discontinuation rate due to adverse events were selected for analysis. Language restriction was not applied. The relevant clinical trials were examined and the data of interest were extracted. Additionally, the risks of bias were also inspected. The efficacy outcomes were the mean changed scores of ADHD rating scales, the overall response rate, and the overall remission rates. The overall discontinuation rate and the discontinuation rate due to adverse events were determined.

Relative risks and weighted mean differences or standardized mean differences (SMDs) with 95% CIs were estimated using a random effect model. A total of 146 subjects in 4 RCTs comparing bupropion with methylphenidate in the treatment of ADHD were included. The pooled mean changed scores of the Iowa-Conner's Abbreviated Parent and Teacher Questionnaires and the ADHD Rating Scale-IV for parents and teachers of children and adolescents with ADHD in the bupropion- and methylphenidate-treated groups were not significantly different. Additionally, the pooled mean changed score in adult ADHD between the 2 groups, measured by the ADHD Rating Scale-IV and the Adult ADHD Rating Scale, was also not significantly different. The pooled rates of response, overall discontinuation, and discontinuation due to adverse events between the 2 groups were not significantly different. The authors concluded that based on limited data from this systematic review, bupropion was as effective as methylphenidate for ADHD patients; tolerability and acceptability were also comparable. However, they stated that these findings should be considered as very preliminary results; further studies in this area are needed to confirm this evidence.

In a Cochrane review, Otasowie (2014) evaluated the effectiveness of tricyclic antidepressants (TCAs) in the reduction of ADHD symptoms within the broad categories of hyperactivity, impulsivity, and inattentiveness in young people aged 6 to 18 years with established diagnoses of ADHD. On September 26, 2013, these investigators searched CENTRAL, Ovid MEDLINE, Embase, PsycINFO, CINAHL, 7 other databases, and 2 trials registers. They also searched the reference lists of relevant
articles, and contacted manufacturers and known experts in the field to determine if there were any ongoing trials or unpublished studies available. Randomized controlled trials, including both parallel group and cross-over study designs, of any dose of TCA compared with placebo or active medication in children or adolescents with ADHD, including those with co-morbid conditions were selected for analysis. Working in pairs, 3 review authors independently screened records, extracted data, and assessed trial quality. They calculated the SMD for continuous data, the odds ratio (OR) for dichotomous data, and 95 % CIs for both. These researchers conducted the meta-analyses using a random-effects model throughout. They used the Cochrane 'Risk of bias' tool to assess the risk of bias of each included trial and the GRADE approach to assess the quality of the body evidence. The authors included 6 RCTs with a total of 216 participants; 5 of the 6 trials compared desipramine with placebo; the remaining trial compared nortriptyline with placebo. One trial compared desipramine with clonidine and placebo, and another compared 2 TCAs (desipramine and clomipramine) with methylphenidate and placebo. Of the 6 trials, 1 RCT primarily assessed the effectiveness of TCA in children with ADHD and co-morbid tic or Tourette disorder, and another 1 trial was in children with co-morbid tic disorder. Randomized controlled trials that met the inclusion criteria varied both in design and quality, and none was free of bias. The quality of the evidence was low to very low according to the GRADE assessments. Tricyclic antidepressants out-performed placebo regarding the proportions of patients achieving a pre-defined improvement of core ADHD symptom severity (OR 18.50, 95 % CI: 6.29 to 54.39, 3 trials, 125 participants, low quality evidence). In particular, there was evidence that desipramine improved the core symptoms of ADHD in children and adolescents as assessed by parents (SMD -1.42, 95 % CI: -1.99 to -0.85, 2 trials, 99 participants, low quality evidence), teachers (SMD -0.97, 95 % CI: -1.66 to -0.28, 2 trials, 89 participants, low quality evidence), and clinicians (OR 26.41, 95 % CI: 7.41 to 94.18, 2 trials, 103 participants, low quality evidence). Nortriptyline was also effective in improving the core symptoms of ADHD in children and adolescents as assessed by clinicians (OR 7.88, 95 % CI: 1.10 to 56.12). Desipramine and placebo were similar on "all-cause treatment discontinuation"
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“reboxe SCOPUS regarding Ghanizadeh children support system the fi most cons vision, e nortriptyline rates. Also, iden iden Toure quality ‐ clonidine low (RD 0.90, 95 % CI: -0.25 to 0.04, 3 trials, 134 participants, very low quality evidence). Desipramine appeared more effective than clonidine in reducing ADHD symptoms as rated by parents (SMD -0.90, 95 % CI: -1.40 to -0.40, 1 trial, 68 participants, very low quality evidence) in participants with ADHD and co-morbid tics or Tourette syndrome. Although this Cochrane Review did not identify serious adverse effects in patients taking TCAs, it did identify mild increases in diastolic blood pressure and pulse rates. Also, patients treated with desipramine had significantly higher rates of appetite suppression compared to placebo, while nortriptyline resulted in weight gain. Other reported adverse effects included headache, confusion, sedation, tiredness, blurred vision, diaphoresis, dry mouth, abdominal discomfort, constipation, and urinary retention. The authors concluded that most evidence on TCAs relates to desipramine. They noted that findings suggested that, in the short-term, desipramine improves the core symptoms of ADHD, but its effect on the cardiovascular system remains an important clinical concern. Thus, evidence supporting the clinical use of desipramine for the treatment of children with ADHD is low.

Ghanizadeh et al (2015) reviewed the available evidence regarding the effectiveness of reboxetine in the treatment of ADHD. The databases of PubMed/Medline, Google scholar, SCOPUS and Web of Science were searched using the keywords: "reboxetine", "ADHD" and "attention deficit hyperactivity disorder". The reference lists of the included studies were screened to find any possible other relevant articles. All the non-controlled and controlled clinical trials were included. The current evidence mainly consists of un-controlled studies, such as case series. Only 3 of 33 studies were controlled clinical trials. They are from single sites and included a sub-sample of patients with ADHD. The author concluded that non-controlled studies and controlled trials support the promising effect of reboxetine in treating ADHD in a sub-sample of patients that are without co-morbid psychiatric disorder and mental retardation. They stated that reboxetine is well-tolerated; however, more controlled trials are needed to reach any firm conclusion.

An UpToDate review on “Attention deficit hyperactivity disorder in
children and adolescents: Overview of treatment and prognosis’ (Krull, 2015a) states that “In addition to elimination diets and fatty acid supplementation, other complementary and alternative (CAM) therapies that have been suggested in the management of ADHD include vision training, megavitamins, herbal and mineral supplements (e.g., St. John’s wort), neurofeedback/biofeedback, chelation, and applied kinesiology, among others. Most of these interventions have not been proven efficacious in blinded randomized controlled trials”.

An UpToDate review on “Attention deficit hyperactivity disorder in children and adolescents: Treatment with medications” (Krull, 2015b) does not mention bupropion, reboxetine, desipramine and nortriptyline as therapeutic options.

There are insufficient data to support sensory integration therapy for ADHD. Sensory integration therapy is a form of therapy in which special exercises are used to strengthen the patient’s sense of balance and to teach the brain to better react and integrate the sensory input it is receiving through structured and constant movement, such as with the use of recreational equipment that spins or rolls.

**SNAP25 Gene Polymorphisms Testing:**

Liu et al (2016) analyzed the possible association between 6 polymorphisms (rs3746544, rs363006, rs1051312, rs8636, rs362549, and rs362998) of SNAP25 and ADHD in a pooled sample of 10 family-based studies and 4 case-control studies by using meta-analysis. The combined analysis results were significant only for rs3746544 (p = 0.010) with mild association (OR = 1.14). Furthermore, the meta-analysis data for rs8636, rs362549, and rs362998 were the first time to be reported; however, no positive association was detected. The authors concluded that there is some evidence supporting the association of SNAP25 to ADHD. Moreover, they stated that future research should emphasize genome-wide association studies in more specific subgroups and larger independent samples.

**Acupuncture:**
Ni and colleagues (2015) evaluated the safety and effectiveness of acupuncture in treating children with ADHD. These researchers performed a literature search to retrieve RCTs of acupuncture in treating ADHD covering the period of the years of establishment of the databases to January 2014 from database of CBM, CNKI, PubMed, Cochrane Library by using key words "attention deficit hyperactivity disorder", "hyperactivity", "minimal brain dysfunction", and "acupuncture". Two independent researchers extracted data from located articles in a pre-defined structured way, and consulted the third researcher if necessary. A total of 13 original trials including 1,304 cases of children with ADHD were obtained in this study. In these trials, acupuncture intervention alone, or acupuncture plus pharmacotherapy (methylphenidate (Ritalin), haloperidol) or acupuncture plus behavioral therapy were compared with simple pharmacotherapy or behavioral therapy alone. Results of the meta-analysis indicated that the total effective rate and Conners' index of hyperactivity (CIH) score-reduction rate in the acupuncture group were significantly superior to those of the other treatment groups [OR = 2.22, 95 % CI: 1.65 to 3.00], Z = 5.22, p < 0.00001] [SMD = -0.94, 95 % CI: -1.41 to -0.47], Z = 3.89, p < 0.0001]. Acupuncture treatment was more effective than haloperidol in reducing the score of Conners' Rating Scale for ADHD [SMD = -7.28, 95 % CI: -8.32 to -6.23), Z = 13.62, p < 0.00001]. Acupuncture was similarly effective as methylphenidate in improving the Chinese medicine syndrome (liver-kidney yin hypo-activity) of children with ADHD [SMD = -1.14, 95 % CI: -2.53 to 0.25), Z = 1.60, p = 0.11]. Less severe adverse effects were reported with acupuncture therapy than the pharmacotherapy (poor appetite, dry mouth, nausea and constipation). These effects were not likely due to publication bias (approximately symmetry funnel plot, Egger's test p > 0.1). The authors concluded that acupuncture is an effective and safe therapy in treating ADHD, combined administration of acupuncture and pharmacotherapy or behavioral therapy is more effective than the pharmacotherapy or behavioral therapy alone. However, they stated that more rigorously designed and high-quality RCTs are needed to confirm the above conclusion.

Mineral Supplementation:
Hariri and Azadbakht (2015) reviewed the evidence regarding the effects of minerals in prevention and management of ADHD. These investigators searched PubMed/Medline, Google Scholar, Ovid, Scopus, and ISI web of science up to June 2013. "iron", "iron supplementation", "magnesium", "magnesium supplementation", "zinc", "zinc supplementation", and "attention deficit hyperactivity disorder" were used as the keywords. A total of 11 RCTs were eligible to be included in the systematic review. This review showed that there is no predominant evidence regarding the use of mineral supplementation on children with ADHD. The authors concluded that there is a need for more evidence for indicating the effect of iron, magnesium, and zinc supplementation in the treatment of ADHD among children.

**Vayarin (Phosphatidylserine-Containing Omega3 Long-Chain Polyunsaturated Fatty Acids):**

In a double-blind, placebo-controlled trial, Manor et al (2012) examined the safety and effectiveness of phosphatidylserine (PS)-containing omega3 long-chain polyunsaturated fatty acids attached to its backbone (PS-Omega3) in reducing ADHD symptoms in children. This 15-week, double-blind, placebo-controlled phase was followed by an open-label extension of additional 15 weeks. A total of 200 ADHD children were randomized to receive either PS-Omega3 or placebo, out of them, 150 children continued into the extension. Efficacy was assessed using Conners’ parent and teacher rating scales (CRS-P,T), Strengths and Difficulties Questionnaire (SDQ), and Child Health Questionnaire (CHQ). Safety evaluation included adverse events monitoring. The key finding of the double-blind phase was the significant reduction in the Global:Restless/impulsive subscale of CRS-P and the significant improvement in Parent impact-emotional (PE) subscale of the CHQ, both in the PS-Omega3 group. Exploratory subgroup analysis of children with a more pronounced hyperactive/impulsive behavior, as well as mood and behavior-dysregulation, revealed a significant reduction in the ADHD-Index and hyperactive components. Data from the open-label extension indicated sustained efficacy for children who continued to receive PS-Omega3. Children that switched to PS-Omega3 treatment from placebo showed a significant reduction
in subscales scores of both CRS-P and the CRS-T, as compare to baseline scores. The treatment was well-tolerated. The authors concluded that the findings of this 30-week study suggested that PS-Omega3 may reduce ADHD symptoms in children. They stated that preliminary analysis suggested that this treatment may be especially effective in a subgroup of hyperactive-impulsive, emotionally and behaviorally-dysregulated ADHD children. Moreover, they stated that the observations of this study were encouraging and could assist in planning future large-scale, placebo-controlled trials evaluating the effectiveness of PS-omega3 in ADHD children.

The main drawbacks of this study were: (i) in the double-blind phase, no superiority was obtained in the primary outcome measure CRS-T, (ii) the subgroup analysis was not planned prior to study initiation, rather it was conducted following significant interactions found; (iii) in the open-label extension phase, there is the lack of a corresponding placebo controlled group and the relatively high percentage of missing data in the CRS-T, due primarily to summer vacation during which teachers could not rate the participants’ behavior, (iv) because of the exploratory nature of the study, these researchers chose not to correct for multiple testing.

An UpToDate review on “Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis” (Krull, 2016) states that “Essential fatty acid supplementation -- We do not suggest essential fatty acid supplementation for children with ADHD. Some studies have noted decreased fatty acid concentrations in the serum of children with ADHD. However, evidence that fatty acid supplementation improves core symptoms in children with ADHD is limited. In a 2012 meta-analysis of randomized and quasi-randomized trials comparing omega-3 and/or omega-6 fatty acid with placebo supplementation in children with ADHD (diagnosed with validated criteria), there were no differences in parent- or teacher-rated ADHD symptoms (overall), inattention, or hyperactivity/impulsivity. Pooled analysis of two small trials (97 participants) found some evidence of improvement in overall ADHD symptoms or parent-rated ADHD symptoms among
children supplemented with both omega-3 and omega-6 fatty acids (risk ratio 2.19 95% CI 1.04 to 4.62). Few of the studies included in the meta-analysis were of high quality. Methodologic limitations included small sample size, variable inclusion criteria, variable type and dose of supplement, and short duration of follow-up. In a 2011 meta-analysis of 10 randomized trials (699 participants), omega-3-fatty acid supplementation was associated with improved ADHD symptoms in children with a diagnosis of ADHD or symptoms of ADHD. The effect size was small to moderate compared with that of pharmacologic therapies (0.31 versus approximately 1.0 and 0.7, respectively). Possible explanations for the variable findings in the two meta-analyses include differences in population (children diagnosed with ADHD versus children with ADHD diagnosis or symptoms) and outcome measures (separate versus pooled parent- and teacher-reported symptoms)“.

Electroencephalography Theta/Beta Power Ratio for the Diagnosis of ADHD:

On behalf of the American Academy of Neurology (AAN), Gloss and colleagues (2016) evaluated the evidence for EEG theta/beta power ratio for diagnosing, or helping to diagnose, ADHD. These researchers identified relevant studies and classified them using American Academy of Neurology (AAN) criteria. Two Class I studies assessing the ability of EEG theta/beta power ratio and EEG frontal beta power to identify patients with ADHD correctly identified 166 of 185 participants. Both studies evaluated theta/beta power ratio and frontal beta power in suspected ADHD or in syndromes typically included in an ADHD differential diagnosis. A bi-variate model combining the diagnostic studies showed that the combination of EEG frontal beta power and theta/beta power ratio has relatively high sensitivity and specificity but is insufficiently accurate. The authors concluded that it is unknown whether a combination of standard clinical examination and EEG theta/beta power ratio increases diagnostic certainty of ADHD compared with clinical examination alone.

AAN Recommendation:
 Clinicians should inform patients with suspected ADHD and their families that the combination of EEG theta/beta power ratio and frontal beta power should not replace a standard clinical evaluation. There is a risk for significant harm to patients from ADHD mis-diagnosis because of the unacceptably high false-positive diagnostic rate of EEG theta/beta power ratio and frontal beta power. (Level B recommendation: Indicates a recommendation that “should” be done)

 Clinicians should inform patients with suspected ADHD and their families that the EEG theta/beta power ratio should not be used to confirm an ADHD diagnosis or to support further testing after a clinical evaluation, unless such diagnostic assessments occur in a research setting. (Level R recommendation: Should be applied only in research settings)

In an editorial that accompanied the afore-mentioned study, Ewen (2016) stated that “Whether TBR (the theta:beta ratio) specifically withstands the test of replication .... We can hope that solid experimental design will prove or disprove the utility of these techniques with little controversy”.

*Evaluation of Iron Status (e.g., Measurement of Serum Iron and Ferritin Levels):*

Wang and colleagues (2017) stated that ADHD is one of the most common psychiatric disorders in children. However, the pathogenesis of ADHD remains unclear. Iron, an important trace element, is implicated in brain function and dopaminergic activity. Recent studies have investigated the association between iron deficiency and ADHD, but the results are inconsistent. These researchers performed a systemic search of Medline, Embase, Web of Science and Cochrane Library databases was supplemented by manual searches of references of key retrieved articles. Study quality was evaluated using the Newcastle-Ottawa Scale. The SMD and 95 % CIs were calculated using a random-effects model. H2 and I2 were used to evaluate the heterogeneity, and sensitivity, subgroup and meta-regression analyses were conducted to explore the reason of heterogeneity. The search yielded 11 studies published before July 25, 2016. Of
these, 10 studies, comprising 2,191 participants and 1,196 ADHD cases, reported serum ferritin levels, and 6 studies, comprising 617 participants and 369 ADHD cases, reported serum iron levels. Serum ferritin levels were lower in ADHD cases (SMD = -0.40, 95 % CI: -0.66 to -0.14). However, these investigators found no correlation between serum iron levels and ADHD (SMD = -0.026, 95 % CI: -0.29 to 0.24). Meta-regression analysis indicated that publication year, age, gender, sample size, and hemoglobin levels did not significantly influence the pooled estimates of serum ferritin. The authors concluded that the findings of this meta-analysis showed that serum ferritin levels were lower in patients with ADHD than in healthy controls, which suggested that serum ferritin is correlated with ADHD. However, these investigators failed to find a correlation between serum iron and ADHD. This is likely due to the fact that serum iron is affected by various factors that were not completely considered in the included studies. The authors noted that there is a need for more high-quality studies with larger sample sizes, assessed using the same assay techniques, and multiple indices of iron status to provide more conclusive results; the mechanisms leading to iron deficiency in ADHD, and the correlation between brain iron and peripheral iron levels also needs further research.

Pharmacogenetic Testing of Drug Response in Individuals with ADHD:

Park et al (2013) examined the associations between the MspI and Dral polymorphisms of the alpha-2 A-adrenergic receptor gene (ADRA2A) and treatment response to methylphenidate according to subtype of ADHD. These researchers enrolled 115 medication-naïve children with ADHD into an open label 8-week trial of methylphenidate. The participants were genotyped and evaluated using the Clinical Global Impression (CGI), ADHD rating scale, and Continuous Performance Test (CPT) pre- and post-treatment. There was no statistically significant association between the MspI or Dral genotypes and the relative frequency of CGI-improvement (CGI-I) 1 or 2 status among any of the groups (all types of ADHD, ADHD-C, or ADHD-I). However, among the children with ADHD-C, those subjects with the C/C genotype at the ADRA2A Dral polymorphism tended to have a CGI-I 1 or 2
status post-treatment (odds ratio [OR] 4.45, p = 0.045). The authors concluded that the findings of this study did not support the association between the Mspl or Dral genotypes and treatment response to methylphenidate in ADHD. However, the results suggested that subtypes might influence pharmacogenetic results in ADHD.

Hegvik et al (2016) noted that ADHD is a common childhood onset neuropsychiatric disorder with a complex and heterogeneous symptomatology. Persistence of ADHD symptoms into adulthood is common. Methylphenidate (MPH) is a widely prescribed stimulant compound that may be effective against ADHD symptoms in children and adults. However, MPH does not exert satisfactory effect in all patients. Several genetic variants have been proposed to predict either treatment response or adverse effects of stimulants. These investigators conducted a literature search to identify previously reported variants associated with MPH response and additional variants that were biologically plausible candidates for MPH response. The response to MPH was assessed by the treating clinicians in 564 adult ADHD patients and 20 genetic variants were successfully genotyped. Logistic regression was used to test for association between these polymorphisms and treatment response. Nominal associations (p < 0.05) were meta-analyzed with published data from previous comparable studies. In this analyses, rs1800544 in the ADRA2A gene was associated with MPH response at a nominal significance level (OR 0.560, 95% confidence interval [CI]: 0.329 to 0.953, p = 0.033). However, this finding was not affirmed in the meta-analysis. No genetic variants revealed significant associations after correction for multiple testing (p < 0.00125). The authors concluded that these findings suggested that none of the studied variants are strong predictors of MPH response in adult ADHD as judged by clinician ratings, potentially except for rs1800544. They stated that pharmacogenetic testing in routine clinical care is not supported by this analyses; further studies on the pharmacogenetics of adult ADHD are needed.

Kim and colleagues (2016) examined the possible association between 2 NMDA subunit gene polymorphisms (GRIN2B rs2284411 and GRIN2A rs2229193) and treatment response to
methylphenidate (MPH) in ADHD. A total of 75 ADHD patients aged 6 to 17 years underwent 6 months of MPH administration. Treatment response was defined by changes in scores of the ADHD-IV Rating Scale (ADHD-RS), clinician-rated Clinical Global Impression-Improvement (CGI-I), and CPT. The association of the GRIN2B and GRIN2A polymorphisms with treatment response was analyzed using logistic regression analyses. The GRIN2B rs2284411 C/C genotype showed significantly better treatment response as assessed by ADHD-RS inattention (p = 0.009) and CGI-I scores (p = 0.009), and there was a nominally significant association in regard to ADHD-RS hyperactivity-impulsivity (p = 0.028) and total (p = 0.023) scores, after adjusting for age, sex, IQ, baseline Clinical Global Impression-Severity (CGI-S) score, baseline ADHD-RS total score, and final MPH dose. The GRIN2B C/C genotype also showed greater improvement at the CPT response time variability (p < 0.001). The GRIN2A G/G genotype was associated with a greater improvement in commission errors of the CPT compared to the G/A genotype (p = 0.001). The authors concluded that these results suggested that the GRIN2B rs2284411 genotype may be an important predictor of MPH response in ADHD.

Furthermore, an UpToDate review on “Attention deficit hyperactivity disorder in children and adolescents: Treatment with medications” does not mention pharmacogenetic testing.

Appendix

*DSM-5 Criteria for ADHD

A. Either 1 or 2:

1. Five or more (17 years of age or older) or six or more (under 17 years of age) of the following symptoms of inattention have been present for at least six months to a point that is disruptive and inappropriate for developmental level:

   Inattention
a. Often does not give close attention to details or makes careless mistakes in schoolwork, work or other activities

b. Often has trouble keeping attention on tasks or play activities

c. Often does not seem to listen when spoken to directly

d. Often does not follow instructions and fails to finish schoolwork, chores or duties in the workplace (not due to oppositional behavior or failure to understand instructions)

e. Often has trouble organizing tasks and activities

f. Often avoids, dislikes or doesn't want to do things that take a lot of mental effort for a long period of time (such as schoolwork or homework)

g. Often loses things needed for tasks and activities (eg, toys, school assignments, pencils, books or tools)

h. Is often easily distracted

i. Is often forgetful in daily activities

2. Five or more (17 years of age or older) or six or more (under 17 years of age) of the following symptoms of hyperactivity-impulsivity have been present for at least six months to an extent that is disruptive and inappropriate for developmental level:

Hyperactivity-impulsivity

a. Often fidgets with hands or feet or squirms in seat

b. Often gets up from seat when remaining in seat is expected
c. Often has trouble playing or enjoying leisure activities quietly (in adolescents or adults this may be reported as "feeling restless")

d. Often "on the go" or often acts as if "driven by a motor"

e. Often talks excessively

f. Often runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless)

g. Often blurts out answers before questions have been finished

h. Often has trouble waiting one's turn

i. Often interrupts or intrudes on others (eg, butts into conversations or games)

B. Some symptoms that cause impairment were present before age 12 years

C. Some impairment from the symptoms is present in two or more settings (eg, at school/work and at home)

D. There must be clear evidence of significant impairment in social, school or work functioning

E. DSM-5 includes no exclusion criteria for people with autism spectrum disorder, since symptoms of both disorders co-occur. However, ADHD symptoms must occur exclusively during the course of schizophrenia or another psychotic disorder and must not be better explained by another mental disorder, such as a depressive or bipolar disorder, anxiety disorder, dissociative disorder, personality disorder or substance intoxication or withdrawal.
# CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

## CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>90791</td>
<td>Psychiatric diagnostic evaluation</td>
</tr>
<tr>
<td>90792</td>
<td>Psychiatric diagnostic evaluation with medical services</td>
</tr>
<tr>
<td>96150</td>
<td>Health and behavior assessment (e.g., health-focused clinical interview, behavioral observations, psychophysiological monitoring, health-oriented questionnaires), each 15 minutes face-to-face with the patient; initial assessment</td>
</tr>
<tr>
<td>96151</td>
<td>re-assessment</td>
</tr>
<tr>
<td>96152</td>
<td>Health and behavior intervention, each 15 minutes, face-to-face; individual</td>
</tr>
<tr>
<td>96153</td>
<td>group (2 or more patients)</td>
</tr>
<tr>
<td>96154</td>
<td>family (with the patient present)</td>
</tr>
</tbody>
</table>

## CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0333T</td>
<td>Visual evoked potential, screening of visual acuity, automated</td>
</tr>
<tr>
<td>0359T - 0374T</td>
<td>Adaptive behavior assessments and treatments</td>
</tr>
<tr>
<td>70450</td>
<td>Computed tomography, head or brain; without contrast material</td>
</tr>
<tr>
<td>70460</td>
<td>with contrast material(s)</td>
</tr>
<tr>
<td>70470</td>
<td>without contrast material, followed by contrast material(s) and further sections</td>
</tr>
<tr>
<td>70496</td>
<td>Computed tomographic angiography, head, with contrast material(s), including noncontrast images, if performed, and image post-processing</td>
</tr>
<tr>
<td>70544</td>
<td>Magnetic resonance angiography, head; without contrast material(s)</td>
</tr>
<tr>
<td>70545</td>
<td>with contrast material(s)</td>
</tr>
<tr>
<td>70546</td>
<td>without contrast material(s), followed by contrast material(s) and further sections</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>70551</td>
<td>Magnetic resonance (e.g., proton) imaging, brain (including brain stem); without contrast material</td>
</tr>
<tr>
<td>70552</td>
<td>with contrast material(s)</td>
</tr>
<tr>
<td>70553</td>
<td>without contrast material, followed by contrast material(s) and further sequences</td>
</tr>
<tr>
<td>70554</td>
<td>Magnetic resonance imaging, brain, functional MRI; including test selection and administration of repetitive body part movement and/or visual stimulation, not requiring physician or psychologist administration</td>
</tr>
<tr>
<td>70555</td>
<td>requiring physician or psychologist administration of entire neurofunctional testing</td>
</tr>
<tr>
<td>76390</td>
<td>Magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>78600</td>
<td>Brain imaging, less than 4 static views</td>
</tr>
<tr>
<td>78601</td>
<td>with vascular flow</td>
</tr>
<tr>
<td>78605</td>
<td>Brain imaging, minimum 4 static views</td>
</tr>
<tr>
<td>78606</td>
<td>with vascular flow</td>
</tr>
<tr>
<td>78607</td>
<td>Brain imaging, tomographic (SPECT)</td>
</tr>
<tr>
<td>78608</td>
<td>Brain imaging, positron emission tomography (PET); metabolic evaluation</td>
</tr>
<tr>
<td>78609</td>
<td>perfusion evaluation</td>
</tr>
<tr>
<td>82784</td>
<td>Gammaglobulin (immunoglobulin); IgA, IgD, IgG, IgM, each [assessment test for prescription of diet]</td>
</tr>
<tr>
<td>82787</td>
<td>Immunoglobulin subclasses (ed, IgG1, 2, 3, or 4), each [assessment test for prescription of diet]</td>
</tr>
<tr>
<td>84630</td>
<td>Zinc</td>
</tr>
<tr>
<td>86001</td>
<td>Allergen specific IgG quantitative or semiquantitative, each allergen [assessment test for prescription of diet]</td>
</tr>
<tr>
<td>88318</td>
<td>Determinative histochemistry to identify chemical components (e.g., copper, zinc)</td>
</tr>
<tr>
<td>90832</td>
<td>Psychotherapy, 30 minutes with patient and/or family member</td>
</tr>
<tr>
<td>90833</td>
<td>Psychotherapy, 30 minutes with patient and/or family member when performed with an evaluation and management service</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>90834</td>
<td>Psychotherapy, 45 minutes with patient and/or family member</td>
</tr>
<tr>
<td>90836</td>
<td>Psychotherapy, 45 minutes with patient and/or family member when performed with an evaluation and management service</td>
</tr>
<tr>
<td>90837</td>
<td>Psychotherapy, 60 minutes with patient and/or family member</td>
</tr>
<tr>
<td>90838</td>
<td>Psychotherapy, 60 minutes with patient and/or family member when performed with an evaluation and management service</td>
</tr>
<tr>
<td>90867</td>
<td>Therapeutic repetitive transcranial magnetic stimulation treatment; planning</td>
</tr>
<tr>
<td>90868</td>
<td>delivery and management, per session</td>
</tr>
<tr>
<td>90869</td>
<td>subsequent motor threshold re-determination with delivery and management</td>
</tr>
<tr>
<td>90875</td>
<td>Individual psychophysiological therapy incorporating biofeedback training by any modality (face-to-face with the patient), with psychotherapy (eg, insight oriented, behavior modifying or supportive psychotherapy); 30 minutes</td>
</tr>
<tr>
<td>90876</td>
<td>45 minutes</td>
</tr>
<tr>
<td>92065</td>
<td>Orthoptic and/or pleoptic training, with continuing medical direction and evaluation</td>
</tr>
<tr>
<td>92537 - 92538</td>
<td>Caloric vestibular test with recording, bilateral; bithermal or monothermal</td>
</tr>
<tr>
<td>92540</td>
<td>Basic vestibular evaluation, includes spontaneous nystagmus test with eccentric gaze fixation nystagmus, with recording, positional nystagmus test, minimum of 4 positions, with recording, optokinetic nystagmus test, bidirectional foveal and peripheral stimulation, with recording, and oscillating tracking test, with recording</td>
</tr>
<tr>
<td>92541</td>
<td>Spontaneous nystagmus test, including gaze and fixation nystagmus, with recording</td>
</tr>
<tr>
<td>92542</td>
<td>Positional nystagmus test, minimum of 4 positions, with recording</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>92544</td>
<td>Optokinetic nystagmus test, bidirectional, foveal or peripheral stimulation, with recording</td>
</tr>
<tr>
<td>92545</td>
<td>Oscillating tracking test, with recording</td>
</tr>
<tr>
<td>92546</td>
<td>Sinusoidal vertical axis rotational testing</td>
</tr>
<tr>
<td>+ 92547</td>
<td>Use of vertical electrodes (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>92548</td>
<td>Computerized dynamic posturography</td>
</tr>
<tr>
<td>92550</td>
<td>Tympanometry and reflex threshold measurements</td>
</tr>
<tr>
<td>92558</td>
<td>Evoked otoacoustic emissions, screening (qualitative measurement of distortion product or transient evoked otoacoustic emissions), automated analysis</td>
</tr>
<tr>
<td>92567</td>
<td>Tympanometry (impedance testing)</td>
</tr>
<tr>
<td>92568 - 92569</td>
<td>Acoustic reflex testing</td>
</tr>
<tr>
<td>92570</td>
<td>Acoustic immittance testing, includes typanometry (impedance testing), acoustic reflex threshold testing, and acoustic reflex decay testing</td>
</tr>
<tr>
<td>92585</td>
<td>Auditory evoked potentials for evoked response audiometry and/or testing of the central nervous system; comprehensive</td>
</tr>
<tr>
<td>92586</td>
<td>limited</td>
</tr>
<tr>
<td>92587</td>
<td>Evoked otoacoustic emissions; limited (single stimulus level, either transient or distortion products)</td>
</tr>
<tr>
<td>92588</td>
<td>comprehensive or diagnostic evaluation (comparison of transient and/or distortion product otoacoustic emissions at multiple levels and frequencies)</td>
</tr>
<tr>
<td>95803</td>
<td>Actigraphy testing, recording, analysis, interpretation, and report (minimum of 72 hours to 14 consecutive days of recording)</td>
</tr>
<tr>
<td>95812</td>
<td>Electroencephalogram (EEG) extended monitoring; 41-60 minutes [covered only for persons with signs of seizure disorder or degenerative neurological condition]</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>95813</td>
<td>greater than 1 hour [covered only for persons with signs of seizure disorder or degenerative neurological condition]</td>
</tr>
<tr>
<td>95816</td>
<td>Electroencephalogram (EEG); including recording awake and drowsy [covered only for persons with signs of seizure disorder or degenerative neurological condition]</td>
</tr>
<tr>
<td>95819</td>
<td>including recording awake and asleep [covered only for persons with signs of seizure disorder or degenerative neurological condition]</td>
</tr>
<tr>
<td>95925</td>
<td>Short-latency somatosensory evoked potential study, stimulation of any/all peripheral nerves or skin sites, recording from the central nervous system; in upper limbs</td>
</tr>
<tr>
<td>95926</td>
<td>in lower limbs</td>
</tr>
<tr>
<td>95927</td>
<td>in the trunk or head</td>
</tr>
<tr>
<td>95928</td>
<td>Central motor evoked potential study (transcranial motor stimulation); upper limbs</td>
</tr>
<tr>
<td>95929</td>
<td>lower limbs</td>
</tr>
<tr>
<td>95930</td>
<td>Visual evoked potential (VEP) testing central nervous system, checkerboard or flash</td>
</tr>
<tr>
<td>95954</td>
<td>Pharmacological or physical activation requiring physician attendance during EEG recording of activation phase (eg, thiopental activation test)</td>
</tr>
<tr>
<td>95957</td>
<td>Digital analysis of electroencephalogram (EEG) (eg, for epileptic spike analysis) [neuropsychiatric EEG based assessment aid (NEBA)]</td>
</tr>
<tr>
<td>96020</td>
<td>Neurofunctional testing selection and administration during noninvasive imaging functional brain mapping, with test administered entirely by a physician or other qualified health care professional (ie, psychologist), with review of test results and report</td>
</tr>
<tr>
<td>96101-96103</td>
<td>Psychological testing</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>96105</td>
<td>Assessment of aphasia (includes assessment of expressive and receptive speech and language function, language comprehension, speech production ability, reading, spelling, writing, e.g., by Boston Diagnostic Aphasia Examination) with interpretation and report, per hour</td>
</tr>
<tr>
<td>96116 - 96125</td>
<td>Neuropsychological testing</td>
</tr>
<tr>
<td>96902</td>
<td>Microscopic examination of hairs plucked or clipped by the examiner (excluding hair collected by the patient) to determine telogen and anagen counts, or structural hair shaft abnormality</td>
</tr>
<tr>
<td>97530</td>
<td>Therapeutic activities, direct (one-on-one) patient contact (use of dynamic activities to improve functional performance), each 15 minutes</td>
</tr>
<tr>
<td>97532</td>
<td>Development of cognitive skills to improve attention, memory, problem solving (includes compensatory training), direct (one-on-one) patient contact, each 15 minutes</td>
</tr>
<tr>
<td>97533</td>
<td>Sensory integrative techniques to enhance sensory processing and promote adaptive responses to environmental demands, direct (one-on-one) patient contact by the provider, each 15 minutes</td>
</tr>
<tr>
<td>97810 - 97814</td>
<td>Acupuncture</td>
</tr>
<tr>
<td>98940</td>
<td>Chiropractic manipulative treatment (CMT); spinal, 1-2 regions</td>
</tr>
<tr>
<td>98941</td>
<td>spinal, 3-4 regions</td>
</tr>
<tr>
<td>98942</td>
<td>spinal, 5 regions</td>
</tr>
<tr>
<td>98943</td>
<td>extraspinal, 1 or more regions</td>
</tr>
<tr>
<td><strong>Other CPT codes related to the CPB:</strong></td>
<td></td>
</tr>
<tr>
<td>83655</td>
<td>Lead level</td>
</tr>
<tr>
<td>96127</td>
<td>Brief emotional/behavioral assessment (eg, depression inventory, attention-deficit/hyperactivity disorder [ADHD] scale), with scoring and documentation, per standardized instrument</td>
</tr>
<tr>
<td>HCPCS Code</td>
<td>Description</td>
</tr>
<tr>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>96365 - 96368</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug)</td>
</tr>
</tbody>
</table>

**HCPCS codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A9583</td>
<td>Injection, Gadofosveset Trisodium, 1 ml [Ablavar, Vasovist]</td>
</tr>
<tr>
<td>A9585</td>
<td>Injection, gadobutrol, 0.1 ml</td>
</tr>
<tr>
<td>G0176</td>
<td>Activity therapy, such as music, dance, art or play therapies not for recreation, related to the care and treatment of patient’s disabling mental health problems, per session (45 minutes or more)</td>
</tr>
<tr>
<td>G0295</td>
<td>Electromagnetic therapy, to one or more areas</td>
</tr>
<tr>
<td>H1010</td>
<td>Non-medical family planning education, per session</td>
</tr>
<tr>
<td>H1011</td>
<td>Family assessment by licensed behavioral health professional for state defined purposes</td>
</tr>
<tr>
<td>J0470</td>
<td>Injection, dimercaprol, per 100 mg</td>
</tr>
<tr>
<td>J0600</td>
<td>Injection, edetate calcium disodium, up to 1,000 mg</td>
</tr>
<tr>
<td>J0895</td>
<td>Injection, deferoxamine mesylate, 500 mg</td>
</tr>
<tr>
<td>J3475</td>
<td>Injection, magnesium sulfate, per 500 mg</td>
</tr>
<tr>
<td>J3520</td>
<td>Edetate disodium, per 150 mg</td>
</tr>
<tr>
<td>M0300</td>
<td>IV chelation therapy (chemical endarterectomy)</td>
</tr>
<tr>
<td>P2031</td>
<td>Hair analysis (excluding arsenic)</td>
</tr>
<tr>
<td>S8035</td>
<td>Magnetic source imaging</td>
</tr>
<tr>
<td>S8040</td>
<td>Topographic brain mapping</td>
</tr>
<tr>
<td>S9355</td>
<td>Home infusion, chelation therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem</td>
</tr>
<tr>
<td>S9445</td>
<td>Patient education, not otherwise classified, non-physician provider, individual, per session</td>
</tr>
<tr>
<td>S9446</td>
<td>Patient education, not otherwise classified, non-physician provider, group, per session</td>
</tr>
<tr>
<td>T1018</td>
<td>School-based individualized education program (IEP) services, bundled</td>
</tr>
</tbody>
</table>
ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F90.0 - F90.9</td>
<td>Attention-deficit hyperactivity disorder</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

11. U.S. Department of Health and Human Services, National
Institutes of Health (NIH). Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder. NIH Consens Statement Online. 1998 Nov 16-18; 16(2): 1-37.


30. UK National Health Service (NHS). Is there any information on the diagnosis of attention deficit hyperactivity disorder (ADHD) in adults? ATTRACT Database. Gwent, Wales, UK:


61. Neale BM, Medland SE, Ripke S, et al; Psychiatric GWAS


64. Canadian Agency for Drugs and Technologies in Health (CADTH). Guidelines and Recommendations for ADHD in Children and Adolescents. Summary of Current Evidence. Ottawa, ON; CADTH; October 2011.


77. Krull KR. Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis. Last reviewed February 2013. UpToDate Inc. Waltham, MA.


84. Krull KR. Attention deficit hyperactivity disorder in children and adolescents: Clinical features and evaluation. UpToDate Inc., Waltham, MA. Last reviewed February 2014.


91. Bukstein O. Adult attention deficit hyperactivity disorder in adults: Epidemiology, pathogenesis, clinical features,
course, assessment, and diagnosis. UpToDate Inc., Waltham, MA. Last reviewed February 2015.


93. Krull KR. Attention deficit hyperactivity disorder in children and adolescents: Treatment with medications. UpToDate Inc., Waltham, MA. Last reviewed February 2015b.


100. Krull KR. Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis.


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Amendment to
Aetna Clinical Policy Bulletin Number: CPB 0426 Attention Deficit/Hyperactivity Disorder

There are no amendments for Medicaid.