Clinical Policy Bulletin: Attention Deficit/Hyperactivity Disorder

Number: 0426

Policy

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
- Measurement of blood lead level
- Medical evaluation (complete medical history and physical examination)
- Parent/child interview

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).

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 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
- Computerized EEG (brain mapping or neurometrics (see CPB 0221 - Quantitative EEG (Brain Mapping))
- Computerized tests of attention and vigilance
- Education and achievement testing*
- Electronystagmography (in the absence of symptoms of vertigo or balance dysfunction)
- Event-related potentials (see CPB 0181 - Evoked Potential Studies)
- Functional near-infrared spectroscopy (fNIRS)
- Hair analysis (see CPB 0300 - Hair Analysis)
- IgG blood tests (for prescription of diet)
- Measurement of zinc
- Neuroimaging (e.g., CT, CAT, MRI [including diffusion tensor imaging], PET and SPECT)
- Neuropsychiatric EEG-based assessment aid (NEBA) System
- Otoacoustic emissions (in the absence of signs of hearing loss)
- Quotient ADHD system/test
- 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:

- 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 treatments
- 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)
- 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)
- Iron supplementation
- Megavitamin therapy (see CPB 0388 - Complementary and Alternative Medicine)
- Metronome training (see CPB 0325 - Physical Therapy Services)
- Music therapy (see CPB 0388 - Complementary and Alternative Medicine)
- 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)
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)
Vision therapy
Yoga (see CPB 0388 - Complementary and Alternative Medicine)

* 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.

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. Electroencephalography or neurological consult is indicated only in the presence of focal signs or clinical suggestions of seizure disorder or degenerative condition.

There are insufficient data to support the usefulness of computerized EEG (brain mapping or neurometrics), 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.

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.

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 for 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 randomized 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/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 stopwatch 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. 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.
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 Bruininiks-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 multi-variate 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” (RD -0.10, 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 (2014) 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.

**CPT Codes / HCPCS Codes / ICD-9 Codes**

**CPT codes covered if selection criteria are met:**

90791 - 90792  Psychiatric diagnostic evaluation with and without medical services

90833  Psychotherapy, 30 minutes with patient and/or family member when performed with an evaluation and management service (List
Attention Deficit/Hyperactivity Disorder

separately in addition to the code for primary procedure)

96150  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

96151  re-assessment

96152  Health and behavior intervention, each 15 minutes, face-to-face; individual

96153  group (2 or more patients)

96154  family (with the patient present)

CPT codes not covered for indications listed in the CPB:

0333T  Visual evoked potential, screening of visual acuity, automated

70450  Computed tomography, head or brain; without contrast material

70460  with contrast material(s)

70470  without contrast material, followed by contrast material(s) and further sections

70496  Computed tomographic angiography, head, with contrast material(s), including noncontrast images, if performed, and image post-processing

70544  Magnetic resonance angiography, head; without contrast material(s)

70545  with contrast material(s)

70546  without contrast material(s), followed by contrast material(s) and further sequences

70551  Magnetic resonance (e.g., proton) imaging, brain (including brain stem); without contrast material

70552  with contrast material(s)

70553  without contrast material, followed by contrast material(s) and further sequences

70554  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

70555  requiring physician or psychologist administration of entire neurofunctional testing

76390  Magnetic resonance spectroscopy

78600  Brain imaging, less than 4 static views
78601 with vascular flow
78605 Brain imaging, minimum 4 static views
78606 with vascular flow
78607 Brain imaging, tomographic (SPECT)
78608 Brain imaging, positron emission tomography (PET); metabolic evaluation
78609 perfusion evaluation
82784 Gammaglobulin (immunoglobulin); IgA, IgD, IgG, IgM, each [assessment test for prescription of diet]
82787 Immunoglobulin subclasses (ed, IgG1, 2, 3, or 4), each [assessment test for prescription of diet]
84630 Zinc
86001 Allergen specific IgG quantitative or semiquantitative, each allergen [assessment test for prescription of diet]
88318 Determinative histochemistry to identify chemical components (e.g., copper, zinc)
90832 Psychotherapy, 30 minutes with patient and/or family member
90834 - 90838 Psychotherapy
90867 Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; initial, including cortical mapping, threshold determination, delivery and management
90868 subsequent delivery and management, per session
90869 subsequent motor threshold re-determination with delivery and management
90875 Individual psychophysiological therapy incorporating biofeedback training by any modality (face-to-face with the patient), with psychotherapy (e.g., insight oriented, behavior modifying or supportive psychotherapy); 30 minutes
90876 approximately 45 minutes
92065 Orthoptic and/or pleoptic training, with continuing medical direction and evaluation
92540 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
92541 Spontaneous nystagmus test, including gaze and fixation nystagmus, with recording
Positional nystagmus test, minimum of 4 positions, with recording

Caloric vestibular test, each irrigation (binaural, bithermal stimulation constitutes four tests), with recording

Optokinetic nystagmus test, bidirectional, foveal or peripheral stimulation, with recording

Oscillating tracking test, with recording

Sinusoidal vertical axis rotational testing

Use of vertical electrodes (List separately in addition to code for primary procedure)

Computerized dynamic posturography

Tympanometry and reflex threshold measurements

Evoked otoacoustic emissions, screening (qualitative measurement of distortion product or transient evoked otoacoustic emissions), automated analysis

Tympanometry (impedance testing)

Acoustic reflex testing

Acoustic immittance testing, includes typanometry (impedance testing), acoustic reflex threshold testing, and acoustic reflex decay testing

Auditory evoked potentials for evoked response audiometry and/or testing of the central nervous system; comprehensive

limited

Distortion product evoked otoacoustic emissions; limited evaluation (to confirm the presence or absence of hearing disorder, 3-6 frequencies) or transient evoked otoacoustic emissions, with interpretation and report

comprehensive diagnostic evaluation (quantitative analysis of outer hair cell function by cochlear mapping, minimum of 12 frequencies), with interpretation and report

Actigraphy testing, recording, analysis, interpretation, and report (minimum of 72 hours to 14 consecutive days of recording)

Electroencephalogram (EEG) extended monitoring; 41-60 minutes [covered only for persons with signs of seizure disorder or degenerative neurological condition]

greater than 1 hour [covered only for persons with signs of seizure disorder or degenerative neurological condition]

Electroencephalogram (EEG); including recording awake and drowsy [covered only for persons with signs of seizure disorder or
degenerative neurological condition]

95819 including recording awake and asleep [covered only for persons with signs of seizure disorder or degenerative neurological condition]

95925 Short-latency somatosensory evoked potential study, stimulation of any/all peripheral nerves or skin sites, recording from the central nervous system; in upper limbs

95926 in lower limbs

95927 in the trunk or head

95928 Central motor evoked potential study (transcranial motor stimulation); upper limbs

95929 lower limbs

95930 Visual evoked potential (VEP) testing central nervous system, checkerboard or flash

95954 Pharmacological or physical activation requiring physician attendance during EEG recording of activation phase (eg, thiopental activation test)

95957 Digital analysis of electroencephalogram (EEG) (eg, for epileptic spike analysis) [neuropsychiatric EEG based assessment aid (NEBA)]

96101 - 96103 Psychological testing

96105 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

96116 - 96125 Neuropsychological testing

96902 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

97530 Therapeutic activities, direct (one-on-one) patient contact (use of dynamic activities to improve functional performance), each 15 minutes

97532 Development of cognitive skills to improve attention, memory, problem solving (includes compensatory training), direct (one-on-one) patient contact, each 15 minutes

97533 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

98940 Chiropractic manipulative treatment (CMT); spinal, 1-2 regions
Attention Deficit/Hyperactivity Disorder

Other CPT codes related to the CPB:

- 98941 spinal, 3-4 regions
- 98942 spinal, 5 regions
- 98943 extraspinal, 1 or more regions

**Other CPT codes related to the CPB:**

- 83655 Lead level
- 96127 Brief emotional/behavioral assessment (eg, depression inventory, attention-deficit/hyperactivity disorder [ADHD] scale), with scoring and documentation, per standardized instrument

HCPCS codes not covered for indications listed in the CPB:

- A9583 Injection, Gadofosveset Trisodium, 1 ml [Ablavar, Vasovist]
- A9585 Injection, gadobutrol, 0.1 ml
- G0176 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)
- G0295 Electromagnetic therapy, to one or more areas
- H1010 Non-medical family planning education, per session
- H1011 Family assessment by licensed behavioral health professional for state defined purposes
- P2031 Hair analysis (excluding arsenic)
- S8035 Magnetic source imaging
- S8040 Topographic brain mapping
- S9445 Patient education, not otherwise classified, non-physician provider, individual, per session
- S9446 Patient education, not otherwise classified, non-physician provider, group, per session
- T1018 School-based individualized education program (IEP) services, bundled

ICD-9 codes covered if selection criteria are met:

- 314.00 Attention deficit disorder without mention of hyperactivity
- 314.01 Attention deficit disorder with hyperactivity

Other ICD-9 codes related to the CPB:

- 296.00 - 296.99 Episodic mood disorders
- 298.0 Depressive type psychosis
- 300.00 - 300.01 Anxiety states
Dysthymic disorder

Adjustment disorder with depressed mood

Prolonged depressive reaction

Depressive disorder, not elsewhere classified

Signs and symptoms involving cognition

Other signs and symptoms involving cognition

Other behavioral problems

Counseling for parent-child problem, unspecified (concern about behavior of child; parent-child conflict)

Educational circumstances (dissatisfaction with school environment; educational handicap)

Social maladjustment; cultural deprivation, political, religious, or sex discrimination; social: isolation, persecution

The above policy is based on the following references:


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


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


84. Maneeton N, Maneeton B, Intaprasert S, Woottiluk P. A systematic review of


87. 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.


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