Attention Deficit / Hyperactivity Disorder over the Life Span

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Summary
Attention deficit / hyperactivity disorder (ADHD) is subsumed under disorders beginning in childhood and adolescence. For adulthood, persistence rates of 20–80% have been reported. Thus, ADHD is a chronic disorder that might result in severe impairments over the life span. This review reports on the symptomatology, classification, co-morbidity, and the epidemiology of ADHD over the life span (from childhood to adulthood). Subsequently, ADHD is introduced as a developmental disorder, possible trajectories and risk factors are described. Diagnostic and therapeutic approaches are reported for the different age groups.

Introduction
In the 2 major classification systems, DSM-IV/5 (Diagnostic and Statistical Manual of Mental Disorders [American Psychiatric Association, 2000, 2013]) and ICD-10 (International Classification of Diseases [World Health Organization, 1992]), attention deficit/hyperactivity disorder (ADHD) is listed as a disorder with onset in childhood and adolescence. ADHD has therefore long been considered exclusively as a disorder of childhood and adolescence. Several longitudinal studies conducted in the 1980s and the early 1990s, however, showed that ADHD is very often a chronic condition [Kessler et al., 2005]. The most recent research suggests that persistence rates in adulthood are very heterogeneous depending on the study, ranging from 20 to 80% [Fischer and Barkley, 2007; Steinhausen et al., 2003]. Afflicted adults have an increased risk of lower educational attainment, less career success, greater career instability, more substance abuse and antisocial behavior, as well as interpersonal problems, especially in intimate relationships [Bark-
ley et al., 1996; Eakin et al., 2004; Mannuzza et al., 1993]. Thus, ADHD is a disorder with an onset in childhood which is chronically debilitating and can still have a high requirement for treatment in adulthood.

This paper presents the symptoms, classification, comorbidity, and epidemiology of the disorder, and then enters into greater detail on ADHD as a developmental disorder and suggests diagnostic and therapeutic approaches for the different phases of life.

### Symptoms and Classification

Both the ICD-10 and DSM-IV/5 distinguish the 3 core symptoms: inattention, hyperactivity, and impulsivity. These must exist across situations (e.g., at home and at school in kindergarten) and must appear before the age of 7 (ICD-10/DSM-IV) or currently before age 12 (DSM-5) [American Psychiatric Association, 2013]. The ICD-10 uses the classification ‘Disturbance of Activity and Attention’ (F90.0) if there have been, for at least a 6-month period, a minimum of 6 symptoms of inattention, 3 symptoms of hyperactivity, and 1 symptom of impulsiveness – symptoms that do not match the child’s developmental stage, are inappropriate, and are clinically debilitating. If there are comorbid conduct disorders, the classification ‘Hyperkinetic Conduct Disorder’ is used (F90.1). DSM-IV requires that a total of 6 out of 9 symptoms of inattention (I) and/or hyperactivity/impulsivity (HI) be met; the classification could then be ‘combined subtype’ (≥ 6 I + ≥ 6 HI symptoms), ‘predominantly inattentive subtype’ (≥ 6 I, ≤ 5 HI symptoms), or ‘predominantly hyperactive-impulsive subtype’ (≥ 6 HI, ≤ 5 I symptoms). According to ICD-10/DSM-IV, autism spectrum disorders are an exclusion criterion; that is no longer the case with DSM-5. The criteria underlying ICD-10 and DSM-IV are often inappropriate to adolescents and adults (e.g. ‘frequently fidgets with hands and feet’ or ‘squirms in seat’) and are the result of studies with children [Bell, 2011; Davidson, 2008; Faraone and Antshel, 2008]. For adult ADHD, it should be noted that the motor restlessness typical in childhood often gives way to a feeling of inner restlessness; symptoms of inattention are common, with consequent limitations of executive functions, and disorganization, especially in relation to job requirements; also common are reduced self-esteem/self-confidence and increased emotional instability/reduced emotional control. These symptoms and limitations, typical of adults, are summarized in the Wender Utah Criteria [Wender, 1995; Wender et al., 1981] (table 1).

Although the Wender Utah Criteria have been criticized for certain limitations [Conners et al., 1997], the symptoms and impairments formulated there have been verified by several studies [see Kooij et al., 2010, for a summary]. DSM-5 therefore considers the adult symptoms with regard to the following points:
- For adolescents (age 17 and up) and adults, only 5 rather than 6 symptoms of inattention or hyperactivity/impulsivity are required;
- the list of hyperactive-impulsive symptoms was expanded to 13, which capture the impairment in adults more appropriately;
- the symptom descriptions are more specific behavioral descriptions, which also apply better to some adults;
- the age of onset was extended so that there must be identifiable inattention or hyperactivity/impulsivity before the age of 12 (instead of 7);
- the symptoms must lead to clear impairment, but no longer before age 12.

### Comorbidity

Overall, high comorbidity rates are reported. Up to 70% of the children and adolescents present psychological problems to an extent requiring treatment [reviews: Davidson, 2008; Stein et al., 2011]:
- 60% oppositional behavior disorders
- 35–50% other conduct disorders
- 10–40% affective disorders, especially depressive
- 20–25% anxiety disorders

For specific learning disabilities comorbidity rates of 25–80% are often reported [Jakobson and Kikas, 2007], whereby children with ADHD and comorbid specific learning disabilities are more severely impaired, often have lower intelligence quotients (IQ), poor language skills, and generally poor academic achievement [Semrud-Clikeman and Bledsoe, 2011].

In adulthood there is a similarly high comorbidity of up to 75% [Kessler et al., 2006; Kooij et al., 2010; Sobanski and Alm, 2004], especially on Axis I (mood disorders, anxiety disorders, substance

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**Table 1. Wender Utah Criteria**

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<tr>
<td>1. Attention disorder</td>
<td>increased distractibility, forgetfulness, inability to attend to conversations</td>
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<td>2. Motor hyperactivity</td>
<td>restlessness, inability to relax, ‘nervousness’</td>
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<td>3. Affective lability</td>
<td>hours to days of prolonged alternation among very positive, neutral, and depressed moods</td>
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<td>4. Disorganized behavior</td>
<td>inadequate planning and organization of activities, tasks are not brought to conclusion</td>
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<td>5. Affect control</td>
<td>low tolerance of frustration, temper outbreaks</td>
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<td>6. Impulsivity</td>
<td>interruption, impatience, impulsive spending</td>
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<tr>
<td>7. Emotional over-reactivity</td>
<td>excessive or anxious reaction to everyday stressors</td>
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abuse, eating disorders, somatoform disorders, adjustment disorders [Cumyn et al., 2007]), but also Axis II (compulsive, antisocial, and borderline personality disorders [Cumyn et al., 2007; Edvins-
on et al., 2013; van Emmerik-van Oortmerssen et al., 2014]) and somatic disorders [Spencer et al., 2014].

These comorbidities can make the diagnosis much more difficult in children and adolescents as well as adults, and should be considered in the diagnostic process.

Prevalence

Three systematic reviews [Polanczyk and Rohde, 2007; Polanczyk et al., 2014; Roman et al., 2003] and 1 meta-analysis [Willcutt, 2012] conclude that there is a worldwide pooled point prevalence of about 5% for ADHD in children and adolescents, with large variations in the ‘prevalence estimates’. These mainly derive from the diagnostic ‘criteria’ that are used (e.g., if the ICD criteria are stricter than the DSM criteria because the ICD does not include the 3 different subtypes used by the DSM, and therefore more symptoms have to be present in total, see above), the ‘information source’ (e.g., whether the judgments of both parents and teachers are required for a diagnosis across situations, see above), and the ‘impairment criterion’ [Polanczyk and Rohde, 2007; Polanczyk et al., 2014].

Differences can be seen between boys and girls in the studies performed so far, with prevalence rates for boys being overall higher [Ford et al., 2003; Huss et al., 2008]. However, there is evidence that mothers tend to judge boys as having more serious problems and that these gender differences decline when the girls, after early adolescence (~12 years), evaluate their symptoms themselves [Kan et al., 2013].

For adults, prevalence rates of 2.5–5% are reported [reviewed in Bell, 2011; Davidson, 2008; Kessler et al., 2006; Polanczyk and Rohde, 2007; Simon et al., 2009], and the gender ratio is more balanced than in childhood and adolescence. This is related, among other things, to the self-referral of adults and their self-reporting of symptoms [Simon et al., 2009], thus supporting indications of a possible distortion by parental assessment (see above). These international findings were also confirmed in a large representative German prevalence study [De Zwaan et al., 2012]. Women also have more comorbid internalizing disorders, which are furthermore associated with a higher self-referral rate and thus more balanced gender ratios in adulthood [Simon et al., 2009].

ADHD as a Developmental Disorder

It is currently believed that multiple development processes underlie ADHD and that the disease should not be treated as a fixed/static disorder [Sonuga-Barke and Halperin, 2010]. For example, children can be differentiated between those with early versus late onset. Thus, longitudinal studies show that only a small proportion of children with an early onset still have disorders when they reach school age [Lavigne et al., 1998a, 1998b; Mathiesen and Sanson, 2000], whereas the vast majority of cases is diagnosed at school age [Sonuga-Barke and Halperin, 2010]. Furthermore, persistence can be distinguished from the fluctuation of symptoms. For example, 20% of adults who were diagnosed with ADHD as children have persistent symptoms, 20% have stable improvement, and 60% moderate improvements in emotional, school/work, and social adjustment [Spencer et al., 2007]. These findings were confirmed by Lahey and Willcutt [2010] in their over-9-year longitudinal study, which showed strong fluctuations over time in the 3 symptom areas, which sometimes meant that children no longer fulfilled the diagnostic criteria for ADHD, yet they continued to have significant clinical impairment. These findings could explain the sharp fluctuations in persistence rates (see above).

To account for these differences in the development trajectory, 4 theoretical phenotypes of a developmental taxonomy have been presented [Sonuga-Barke and Halperin, 2010]:

- Type I (emergent oppositionality): early sub-clinical ADHD symptoms are a risk factor for developing oppositional defiant disorders, and coercive/negative parenting moderates the development of the disorder.
- Type II (late-onset ADHD): early sub-clinical ADHD symptoms have a clinically significant long-term effect, either because of genetic or environmental factors or due to contextual changes, e.g., if the child enters school.
- Type III (preschool-limited ADHD): early significant clinical symptoms do not have a further negative effect due to protective factors, such as a structured home/school, clear rules and limits, so that the development of the disorder is interrupted.
- Type IV (early-onset chronic ADHD): early chronic symptoms exist since kindergarten age and are accompanied by temperament-based problems with emotion regulation, which in turn reinforce negative parenting and lead to further worsening of the symptoms.

A task for future research is to validate these 4 possible phenotypes, observe them longitudinally, and, if possible, to develop need-based early interventions that could prevent pathological trajectories. Moderators and mediators that influence the trajectory of the disorder should be taken into account. Pre- and perinatal risk factors, genetics, gene-environment interactions, as well as biological, neuropsychological, and environmental moderators are being discussed. Many individual studies and reviews have investigated this, some with well-replicated findings, but sometimes also with very heterogeneous results. An example: it is well-established that ADHD is hereditary and that different genes with small effects contribute to ~76% heritability [review: Faraone et al., 2005]. Yet, the findings about which genes actually influence the incidence and heritability of ADHD are extremely heterogeneous [review: Li et al., 2014]. Findings from epigenetic research also show that environmental factors such as parental hostility and criticism moderate the genetic effect on the severity of ADHD and comorbid conduct disorders [Sonuga-Barke et al., 2008a], although research on the epigenetics of ADHD is still sparse [review: Elia et al., 2012]. Two things follow from this: first, such moderating and mediating fac-
tors in the development of ADHD must be considered; and second, the typical developmental symptoms must be described in great detail so that the developmental types can be correctly identified. This requires a very accurate diagnosis.

**Diagnosis in the Various Phases of Life**

Several guidelines for the diagnosis of ADHD have been published [American Academy of Child and Adolescent Psychiatry, 2007; Taylor et al., 2004; Village, 2011]. All of them recommend the use of a variety of methods and sources of information, such as behavioral observations, parent and teacher questionnaires, standardized interviews, and a somatic survey of findings, for children and for adolescents and adults alike. According to the guidelines of the National Institute for Health and Care Excellence (NICE; www.nice.org.uk/guidance/cg72) [summary: Atkinson and Hollis, 2010], the following recommendations pertain to the diagnosis:

- The diagnosis should only be made by a psychiatrist, pediatrician, or specialist with training and expertise in ADHD;
- ADHD can occur in all age groups and the symptom criteria are age-adjusted to correspond to the behavior;

**Excursus: Neuropsychology of ADHD**

There has been a great number of studies of the neuropsychological deficits in ADHD. In particular, disorders of executive functions (EF), such as lack of inhibition or reduced attention skills, have been detected repeatedly in various studies [reviews: Pennington and Ozonoff, 1996; Willcutt et al., 2005], but also motivation disorders, which contribute to the heterogeneity of ADHD symptoms and are explained by changed motivational processes [Johansen et al., 2002; Sonuga-Barke et al., 2008b]. In this context, Sonuga-Barke developed the dual pathway model [Sonuga-Barke, 2002, 2003, 2005] (fig. Schematic representation of the dual pathway model of ADHD). This assumes, first of all, that there are EF disorders (inhibitory control), which are manifest for example in worse performance in tasks involving reaction control [Chamberlain et al., 2011; Pennington and Ozonoff, 1996; Willcutt et al., 2005]. Thus, children with ADHD tend to react rather more slowly, more variably, are worse at stimulus detection, and make more mistakes [Barkley et al., 1996; Cepeda et al., 2000; Oades and Christiansen, 2005; Willcutt et al., 2005].

The most consistent effects between children with and without ADHD with regard to executive dysfunctions (ED) have been found to have average effect strengths (d = 0.46–0.69) for reaction inhibition, vigilance, working memory, and planning [Willcutt et al., 2005].

Secondly, the dual pathway model assumes a motivational component in children with ADHD, independent of EF disorders, which is linked to fundamental changes in reward mechanisms, particularly to a shortened delayed reward gradient [Sagvolden and Sergeant, 1998; Sagvolden, 2000; Sonuga-Barke, 2002, 2011]. The core symptomatology is thus an expression of delay aversion (DA). This is shown, for example, in the very robust and frequently replicated finding that children with ADHD prefer quick/prompt small rewards rather than later, larger rewards [Antrop et al., 2006; Bitsakou et al., 2009; Dalen et al., 2004; Marco et al., 2009; Solanto et al., 2001]. If they have no way to escape aversive delay, however, they exhibit hyperkinetic behavior, to reduce the aversive feeling that a long and boring period of time has elapsed [Antrop et al., 2000; Sonuga-Barke, 2002].

Empirical checks of this model were able to confirm the underlying theoretical assumptions. The assumed pathways (inhibitory dysfunction vs. DA) are actually independent of one another and the ADHD symptoms on the neuropsychological level as a result of these 2 distinct processes [Dalen et al., 2004; Solanto et al., 2001; Sonuga-Barke, 2002]. One study, which directly compared the postulated neuropsychological deficits (ED vs. DA) with a stop-signal test (ED) and a choice-delay test (DA) in a group of ADHD children, showed that the 2 tests were virtually uncorrelated and comprised 4 distinct groups: 23% of the children showed only inhibitory deficits, 15% showed only DA, 23% showed both inhibitory and motivational deficits, and 39% showed no abnormalities at all [Solanto et al., 2001]. The study also shows that the ADHD symptomatology is clearly heterogeneous and individual neuropsychological profiles are not directly indicative of specific neuropsychological ADHD subtypes, such as an ED subtype and a motivational dysfunction subtype. Nevertheless, both measures (ED and DA) can be used...
to correctly classify up to 90% of children with ADHD, which speaks in favor of also using neuropsychological measures for the diagnosis of ADHD [Solanto et al., 2001].

In the dual pathway model, DA is associated with changes in the mesolimbic system, and ED with changes in the mesocortical system (see above). ED in ADHD could be associated neurobiologically with smaller brain volume, especially with reductions in the frontal lobe, the basal ganglia, and the cerebellum [review: del Campo et al., 2012; Paule et al., 2000]. In the further development of the dual pathway model, Sonuga-Barke et al. [2010] also proposed a triple pathway, which relates to control (timing/temporal processing) (fig. Model of distinct neurobiological pathways that lead to overlapping but separable cognitive profiles and ADHD symptoms). Deficiencies in control with ADHD were associated on the neurobiological level with changes in the cerebellum and on the symptom level especially with motor development delays [Durston et al., 2011; Krain and Castellanos, 2006]. Studies of ADHD and motor development delays provide evidence of high comorbidities of 30–50% [Kadesjö and Gillberg, 2001; Meyer and Sagvolden, 2006]. It was assumed for a long time that the motor impairments with ADHD are a consequence of the core symptoms. Recent studies have shown, however, that this is not the case; rather the motor deficits are independent [reviews: Pitcher et al., 2003; Sergeant et al., 2006]. Several neurological tests have established that children with ADHD differ from healthy control children with regard to repetitive movements, fine motor skills, coordination deficits, and movement control, especially in the absence of visual feedback, poor balance, and the above-mentioned reduced control skills [Sergeant et al., 2006]. Gross motor development deficits were hitherto associated with the combined ADHD subtype, and fine motor deficits with the predominantly inattentive subtype. But also EF deficits, particularly inhibitory dysfunctions, were associated in ADHD with motor development delays [Livesey et al., 2006; Pitcher et al., 2003]. The basal ganglia and the cerebellum are described as the common neurobiological foundation for this. Both are central to the planning, initiation, and execution of movements and behavior, assuming that the inhibitory functions of the basal ganglia complement the excitatory functions of the cerebellum [Livesey et al., 2006; Sergeant et al., 2006]. However, changes in the cerebellum could also be detected in other mental disorders, such as schizophrenia in childhood and adolescence [Greenstein et al., 2011], so that changes in the cerebellum and also most other brain regions are not specific to ADHD [Paule et al., 2000] and deficits in EF as well as motor development are obviously also associated with other factors.

![Model of distinct neurobiological pathways that lead to overlapping but separable cognitive profiles and ADHD symptoms](modified from Durston et al., 2011).

Thus neuropsychological models should encompass deficits not only in 1 area, but, if possible, along the 3 pathways discussed here (EF, DA, timing), so as to arrive at the best possible classification.

- questionnaires alone are not sufficient for a diagnosis; a diagnosis should be based on a clinical psychological assessment, a complete medical history, self-evaluations and informant evaluations (by parents and teachers), including comorbid disorders, possible parental illnesses, as well as an assessment of intellectual abilities;
- a diagnosis should only be made if the diagnostic criteria are met according to DSM or ICD, with at least moderate persisting impairment, and can be observed consistently in different areas of life.

A criticism of these recommendations is that self- and informant-assessments, as well as clinical interviews, are prone to distortion because of underlying subjectivity [Edwards et al., 2007]. In a study by Bruchmüller et al., 1,000 randomly selected practicing child and adolescent psychotherapists/psychiatrists were sent 4 case vignettes describing either a boy or girl [Bruchmüller et al., 2012; Bruchmüller and Schneider, 2012]. In Vignette 1, all ADHD criteria had been met; in Vignette 2 the criteria of occurrence across situations and onset of disease before age 7 were not met; in Vignette 3, other ADHD symptoms were lacking; and Vignette 4 comprised the criteria for Generalized Anxiety Disorder (GAD). In Vignette 1, a total of 80% of the girls and 77% of the boys were classified correctly; but that also means that 20% of the girls and 23% of the boys were not correctly identified as having an illness and therefore would have received no further help. There were false positive classifications for 11% of the girls and 20% of the boys in Vignette 2; for 9% of the girls and 20% of the boys in Vignette 3; and 13% of the girls and 18% of the boys in Vignette 4 (GAD). Overall, the false-positive rate for the boys significantly exceeded the false-negative rate, which is an indication of the over-diagnosis of the boys.

A further source of over-diagnosis can be the age of the children. Thus the studies of Elder [2010], Evans et al. [2010], and Morrow et al. [2012] showed that, compared with the oldest children of a given age group, the youngest children in a school class (e.g., the cut-off
date is September 1, so all children who were born before August 31 must be enrolled for that school year, whereas children who were born after September 1 are enrolled 1 year later) were found to have up to 3 times higher rates of ADHD diagnoses and methylphenidate (MPH) prescriptions [Elder, 2010; Evans et al., 2010; Morrow et al., 2012]. This finding is probably related to a normal and generally high variance in the development of preschool children. At the same time, the early, correct identification of behavioral problems is one of the best ways to stop pathological developments. Insofar as possible, diagnostic procedures should assess both: developmental milestones and possible behavioral problems, the better to evaluate the latter in the context of overall development.

The Conners Early Childhood Scales (Conners EC) were developed with this objective for children aged 2 to 6 [Conners, 2009]; the German adaptation is currently in preparation by H. Christiansen, S. Harbarth, E. Neidhard, and R. Steinmayr, and is expected to be published in the fall of 2016 by the Hogrefe-Verlag. With respect to assessments by parents (190 items) and teachers (186 items), the scales capture social disabilities, behavioral and emotional problems, as well as developmental milestones. It turns out that the various areas of development (adaptive, motor, and pre-academic/cognitive skills, communication, play behavior) are highly correlated with each other (0.70–0.89; p < 0.05). Delays in one area are very likely accompanied by delays in other areas. In addition, there are small to moderate, although significant, correlations among the various developmental milestones and the scale ‘Inattention/Hyperactivity’ (0.25–0.33; p < 0.05), an indication that delays in development may be associated with ADHD-typical behavioral problems [Harbarth and Christiansen, 2015]. In a study with 100 German children, there was likewise a significant relationship between the developmental milestones and the scale of ‘Inattention/Hyperactivity’ in the teachers’ judgment (0.33; p < 0.001), but not in that of the parents [Feuer, 2014]. Overall, there is notably a lack of prospective longitudinal studies that examine behavioral problems while taking into account developmental milestones over time, and which thus might shed light on possible connections.

As already mentioned, girls above the age of 12 give themselves higher problem scores and mothers seem to perceive boys under 12 as having more severe problems [Kan et al., 2013]. There are also large fluctuations in symptoms over time [Lahey and Willcutt, 2010; Rabiner et al., 2010], and gender, ethnicity, and socioeconomic status also affect symptom assessments [Huss et al., 2008]. To complement the diagnosis, therefore, the use of objective, reliable laboratory parameters is recommended, such as neuropsychological testing (see ‘Excursus: Neuropsychology of ADHD’, accompanying this article) [Hasson and Fine, 2012].

Analogous diagnostic recommendations apply to adulthood [review: Haavik et al., 2010]. According to the European Consensus Statement on the Diagnosis and Treatment of Adult ADHD [Kooij et al., 2010], the following gold standard applies:

1) a specific clinical interview and clinical interviews to detect comorbid Axis I and II disorders;
2) standardized questionnaires for assessment of adult ADHD symptoms;
3) if possible, appraisal of school and employer references;
4) neuropsychological diagnosis (see above).

In a study of the diagnosis of adult ADHD, we showed that 27.6% of patients were below the cut-off score of the Amsterdam Short-Term Memory test (ASTM). The ASTM is used to check for the feigning of symptoms [Schmand and Lindeboom, 2005]. While the ASTM in this study did not correlate with the validity scales of the Conners Adult ADHD Rating Scales, there were significant associations with the neuropsychological markers for sustained attention and divided attention [Hirsch and Christiansen, 2015]. It would thus seem that there is a subgroup of adult ADHD patients who suffer from extreme attention disorders. This group has a particularly great need for support and should therefore be diagnosed well recognized.

**Fig. 1.** Risk model of long-term socioeconomic consequences [Schmidt and Petermann, 2011, p 234].

![Image](image-url)
Primary/Universal Approaches

Primary preventive approaches are aimed at healthy individuals; health should be promoted by reducing risk factors and encouraging protective factors and resources. Universal measures are also aimed at the entire population [Röhrle et al., 2012]. An example would be the promotion of maternal health, e.g., by the reduction of tobacco, alcohol, and other substance use, and of exposure to environmental toxins such as lead/mercury during pregnancy, as these have been associated with increased risk of ADHD in children [Nigg, 2012; Halperin et al., 2012].

Since the first ADHD symptoms are often noticed very early (see above) and interventions are more effective when the psychopathology is not fully developed, preventive programs are offered [Daley et al., 2009; Halperin et al., 2012; Sonuga-Barke and Halperin, 2010]. Kindergartens and schools are ideal for universal prevention programs, since they can in principle reach all children on a low-threshold basis and are not stigmatizing [Fowler et al., 2014; Röhrle et al., 2012].

Preschool programs that train the working memory, attention and self-regulation have proven effective in the few studies done so far [Daley et al., 2009; Fabian, 2004; Fowler et al., 2014; Jones et al., 2007, 2008; Plueck et al., 2015; Sonuga-Barke and Halperin, 2010; Thompson et al., 2009]. For example, the following programs were associated with positive effects [Halperin et al., 2012]:

- The Incredible Years Program: an evidence-based program for parents, children and teachers; the goal is the prevention of childhood behavioral problems and promotion of their social, emotional, and academic skills. The program is in use worldwide and its effects have been demonstrated across cultures and social strata (http://incredibleyears.com/).
- Triple P (Positive Parenting Program): promotes the development, health, and social skills of children; prevents problems in emotional, behavioral, and developmental areas; aims to create a non-violent, protective, and nurturing environment for children; changes unfavorable parenting practices and enhances parenting skills; reduces family stress and increases coping skills (www.triplep.net/glo-en/home).
- Revised New Forest Parenting program (RNFP): after psychoeducation about ADHD, parents are instructed how to help their child to be calmer and more receptive. Behavioral techniques are used such as praise, point plans, and time-outs to cope with problem behavior (https://www.jfhc.co.uk/paying_attention_to_adhd_80355.aspx).
- Training Executive, Attention & Motor Skills (TEMS): research program for preschoolers with ADHD, which uses play and physical activity to promote neuronal processes that underlie the core symptoms of ADHD and associated problem areas. The program is combined with parental psychoeducation about ADHD at home and in supervised playgroups (https://clinicaltrials.gov/ct2/show/NCT01073176).
- Enhancing Neurocognitive Growth with the Aid of Games & Exercise (ENGAGE): is intended to promote the self-regulation of preschool children and focuses on behavioral, emotional, and neurocognitive skills, which are practiced for the control of attention, behavior, inhibition, and emotions [Healey and Halperin, 2014].
- Executive Training of Attention & Metacognition (ETAM): training to promote executive functions such as attention, working memory, and self-regulation for preschoolers at risk for ADHD (https://clinicaltrials.gov/ct2/show/NCT01675869).

In a separate study [Christiansen et al., 2015], we compared a group that had received a universal educational behavioral training program with a group that had also received attention training [Fábián, 2004]. It was found that preschool children especially benefited from the pedagogical behavioral modifications, whereas the specific attention training did not reduce ADHD symptoms. A comparison of children with high versus low risk showed that children with more pronounced symptoms especially benefited from the training; no harm was done to the other children – also a key factor in preventive programs.

Therapy Guidelines

The NICE and European guidelines for the treatment of ADHD include the following [Atkinson and Hollis, 2010; Graham et al., 2011]:

- At preschool age, medication is not recommended, but rather training programs for parents and caregivers (see above).
- At school age, medication for moderate ADHD symptoms is likewise not the first choice, but also here behavioral programs are recommended for parents, children, and teachers.
- Medication is recommended for severe symptoms in school-age children.
- In adulthood, drug treatment is the first choice, which may be accompanied by cognitive behavioral therapy (CBT) if the medication does not achieve the desired results or if patients want a psychotherapeutic treatment.

For ADHD therapy with ‘school-age children’, these guidelines take a multimodal approach and recommend that medication be used only in a crisis situation or if behavioral approaches are insufficient. Although this is the recommendation, it does not seem to always correspond to reality. The treatment of children with ADHD is primarily pharmacological, and prescription rates for psychostimulants continue to rise [Dalsgaard et al., 2014; Steinhausen and Bisgaard, 2014]. Although treatment with psychostimulants may be very effective in the short term [Van der Oord et al., 2008], it is not always the most appropriate treatment, since non-responder rates are ~30% [Lofthouse et al., 2012] and aversive side effects like insomnia and loss of appetite are commonly reported [Graham et al., 2011; Surgeon General of the United States, 1999]. In addition, the long-term medical effects have not yet been sufficiently established, and improvements after cessation of psychostimulants are often not durable [Molina et al., 2009]. In the long term, it seems that 44–75% of the children treated with psychostimulants do not benefit satisfactorily from the treatment [Molina et al., 2009]. Protective long-term effects, for example with regard to later substance use [Molina et al., 2009, 2013] or academic success, social and interpersonal skills, have likewise not yet been consistently confirmed [Molina et al., 2009; Mrug et al., 2012; Van de Loo-Neus et al., 2011].
In a separate meta-meta-analysis that examined the existing meta-analyses and reviews on interventions for ADHD, we identified 44 meta-analyses [Christiansen et al., 2014a]. Of these, 34 meta-analyses were for ADHD treatment in children/adolescents; 6 of these were with psychostimulants, 1 with alternative drug treatment approaches, 3 with omega-3 fatty acids, 2 with a combination of psychostimulants and behavioral therapy (CBT), 7 with CBT, and 4 with neurofeedback. The results of the meta-meta-analysis show that treatment with a psychostimulant alone leads to a small, homogeneous, relatively stable effect (standardized mean difference (SMD) 0.36, fail-safe n = 37). CBT alone also leads to a small, homogeneous, but very stable effect (SMD 0.35, fail-safe n = 284), which in the judgment of the parents alone turns out to be slightly higher (SMD 0.44, fail-safe n = 370), and in the judgment of the teacher alone unsatisfactorily small (SMD –0.04), and also unstable (fail-safe n = 0). CBT alone shows average, homogeneous, and relatively stable effects for oppositional defiant disorders and conduct disorders (SMD 0.72, fail-safe n = 21) – the most common comorbid disorders with ADHD, which, also according to the assumed development types (see above), have been associated with an unfavorable trajectory. The combination treatment (psychostimulants + CBT) resulted in a large, homogeneous effect (SMD 1.12), but the number of studies (k = 2) is too small to allow firm conclusions to be drawn. However, since the treatment guidelines recommend ‘stepped care’, it is reasonable, if the treatment outcome is insufficient, to administer the combination treatment. Neurofeedback results in an average, homogeneous, and relatively stable effect (SMD 0.52, fail-safe n = 32), which is better than either stimulants or CBT alone. Treatment with omega-3 fatty acids results in small, but homogeneous and very stable effects (SMD 0.21, fail-safe n = 900). The argument for the superiority of MPH treatment over other therapeutic methods, frequently encountered in clinical practice, does not seem quite justified, given these results. CBT results in comparable effects, but these are not reflected in the teachers’ judgment. But various studies provide evidence that teachers’ judgments may be distorted by lack of knowledge of the disorder [Alkahtani, 2013; Anderson et al., 2012; Bekle, 2004; Ruhmland, 2013; Scuotto et al., 2000] or may show halo effects [Sayal et al., 2010]. Neurofeedback seems to be a possible treatment alternative, as are omega-3 fatty acids, e.g., if there are reservations about psychostimulants.

In a separate study that compares neurofeedback with a self-management training approach, we showed that so far both therapies contribute to a significant reduction in symptoms [Christiansen et al., 2014b]. We believe that, inter alia, the high-frequency treatment (3 times per week) contributes to these effects, as children with ADHD are often distinguished by their reduced tolerance for frustration and prefer quick results (see above, neuropsychological research). Thus, therapy research should not only study various therapy approaches, but also treatment modalities (number of sessions per week, use of token economies, concurrent parent training, inclusion of teachers, treatment of comorbid disorders, medications, etc.).

Treatment rates for ‘adolescents’ decline dramatically, and pharmacological studies are preponderant in the literature on therapy for adolescent ADHD; such studies often confront compliance problems [review: Robb and Findling, 2013; McClain and Burks, 2015]. Separation from the family and from adults, and the development of autonomy, are developmental tasks for adolescents. These development tasks may make a therapeutic process more difficult. Motivational interviewing [Miller and Rose, 2009] has been found to be helpful with adolescents in this regard. In motivational interviewing, reasons for and against a change are discussed and patients are encouraged to become advocates for their own change. Resistance phenomena should be used as sources of information to better define the problem and goal. The principles of motivational interviewing include: express observations only; ask precise questions to be able to understand precisely; slow down and focus on details and emotional significance; do not argue and persuade, but listen; discuss questions and doubts; responsibility and decisions about changes are up to the patient; work out specific goals for change (positive, realistic, attractive); work out specific subgoals along with global objectives [Bolten, 2011]. A randomized controlled trial with adolescents compared neurofeedback combined with Treatment as Usual (TAU; CBT, systemic therapy, counseling, medication) versus TAU alone [Bink et al., 2014]. After the therapy, there were significant improvements in both groups, but no additional effect for neurofeedback. Overall, there is a need for further research about the adolescent years, and psychosocial stress factors should be brought into better focus [Serrano-Troncoso et al., 2013].

According to the European Consensus Statement [Kooij et al., 2010], ‘therapy for adult ADHD’ should be based on 3 building blocks – psychoeducation, pharmacotherapy, and psychotherapy. Our meta-meta-analysis showed that medication (both psychostimulants and other medications such as atomoxetine) in adults results in average, homogeneous, and stable effects (SMD 0.43, fail-safe n = 280), which are equivalent to MPH treatment alone (SMD 0.49, fail-safe n = 56) [Christiansen et al., 2014a]. According to the learning theory model of adult ADHD, patients have negative appraisal styles, which reinforce dysfunctional cognitive convictions and schemata and consequently a cycle of dysfunctional behaviors [Newark et al., 2012; Newark and Stieglitz, 2010]. Based on this model, analogous to promoting the methods of CBT, the promotion of resources and positive coping strategies and managing of cognitive dysfunction are recommended according to the guidelines (see above) – classical CBT approaches, which we assume are well known and will not elaborate here.

In her expert review of therapy for adult ADHD, Philipsen [2012] found that psychoeducation, CBT, as well as dialectical-behavioral and mindfulness-based therapies are generally associated with good treatment outcome (effect sizes > 0.80), which confirms the recommendations of the Consensus Statement (see above) [Philipsen, 2012]. At the University of Tübingen there is currently a large-scale, randomized controlled trial underway to test the effectiveness of neurofeedback in adulthood, in which training of slow cortical potentials is compared with near-infrared spectroscopy (a new form of neurofeedback) and electromyogram feedback as well as a healthy control group [Mayer et al., 2015]. The study is
currently in progress, but if 1 of the 2 neurofeedback treatments proves effective, this would provide another treatment alternative for adult ADHD.

**Conclusion**

In many cases, ADHD is a chronic disorder with heterogeneous and fluctuating symptoms that causes high social costs. The earlier effective interventions are used, the greater the likely long-term effects. Therefore, good screening methods for correct early detection are key; these should particularly take into account the child’s developmental level. There are already some programs for early childhood, with promising effects; however, the vast majority are indicated or selective. Universal programs in kindergartens/schools offer the possibility of reaching almost all children in a low-threshold, non-stigmatizing way, and do not seem to be harmful for children without behavior problems; there is need for further research here.

The various possible developmental types of ADHD are probably based on heterogeneous etiological development pathways, which affect the therapeutic results; further research is urgently needed.

There is a lack of specific programs especially for adolescence, and so far a lack of good therapeutic trials for this age group.

For adults, there is a good international standard for diagnosis and therapy, which has had good results. To reduce the morbidity rate in adulthood, we still need good research into effective early detection and intervention methods.

**Disclosure Statement**

The author declares that there is no conflict of interest concerning this paper.

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**References**


