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Practical considerations for the evaluation and management of Attention Deficit Hyperactivity Disorder (ADHD) in adults

Considérations pratiques pour l'évaluation et la prise en charge du Trouble Déficit de l'Attention/Hyperactivité (TDAH) chez l'adulte

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Practical considerations for the evaluation and management of Attention Deficit Hyperactivity Disorder (ADHD) in adults

Considérations pratiques pour l'évaluation et la prise en charge du Trouble Déficit de l'Attention/Hyperactivité (TDAH) chez l'adulte

ABSTRACT

Attention deficit with or without hyperactivity disorder (ADHD) is one of the most frequent neuropsychiatric disorders, and affects 2-4% of adults. In contrast with many European countries, the identification and management of adult ADHD remains underdeveloped in France, and a subject of controversy. This review provides a practical update on current knowledge about ADHD in adults for French-speaking professionals who have to detect or manage adult patients with ADHD. ADHD is classified as a neurodevelopmental disorder in the recent update of the international diagnostic classification. While symptoms and impairment due to ADHD are frequently severe during childhood, they often evolve as children grow older, with frequent persistent disabilities in adulthood. In adulthood, the clinical presentation, as in childhood, involves the symptom triad of inattention, hyperactivity and impulsivity. However, differences are noted: hyperactivity is more often internalized, symptoms of inattention may be masked by anxiety symptoms or obsessive-like compensation strategies. ADHD is often diagnosed during childhood, but it is not rare for the diagnosis to be made later. Failure to recognise symptoms resulting in misdiagnosis, or alternatively well-developed compensation factors could be two underlying reasons for the long delay until diagnosis. Other symptoms, such as emotional deregulation or executive function-related symptoms are also usually observed in adults. In addition, in adults, ADHD is often associated with other psychiatric disorders (in 80% of cases); this makes the diagnosis even more difficult. These disorders encompass a broad spectrum, from mood disorders (unipolar or bipolar), to anxiety disorders, and other neurodevelopmental disorders and personality disorders, especially borderline and antisocial personality disorder. Substance use disorders are very common, either as a consequence of impulsivity and emotional dysregulation or as an attempt at self-treatment. Sleep disorders, especially restless leg syndrome and hypersomnolence, could share common pathophysiological mechanisms with ADHD. ADHD and comorbidity-related symptoms are responsible for serious functional impairment, in various domains, leading to academic, social, vocational, and familial consequences. The impact on other psychiatric disorders as an aggravating factor should also be considered. The considerable disability and the poorer quality of life among adults with ADHD warrant optimal evaluation and management. The diagnostic procedure for ADHD among adults should be systematic. Once the positive diagnosis is made, the evaluation enables characterisation of the levels of severity and

impairment at individual level. A full examination should also assess medical conditions associated with ADHD, to provide personalized care. In recent years, a growing number of assessment tools have been translated and validated in French providing a wide range of structured interviews and standardized self-report questionnaires for the evaluation of core and associated ADHD symptoms, comorbidities and functional impairment. The treatment of ADHD in adults is multimodal, and aims to relieve the symptoms, limit the burden of the disease, and manage comorbidities. The most relevant and validated psychological approaches are psycho-education, cognitive-behavioural therapy and "third wave therapies" with a specific focus on emotional regulation. Cognitive remediation and neurofeedback are promising strategies still under evaluation. Medications, especially psychostimulants, are effective for alleviating ADHD symptoms with a large effect size. Their safety and tolerance are satisfactory, although their long-term clinical benefit is still under discussion. In France, methylphenidate is the only stimulant available for the treatment of ADHD. Unfortunately, there is no authorization for its use among adults except in continuation after adolescence. Hence the prescription, which is subject to the regulations on narcotics, is off-label in France. This article aims to provide practical considerations for the management of ADHD and associated disorders in adults, in this particular French context.

Keywords: *Adult ADHD, diagnosis, treatment, comorbidity, methylphenidate, psychotherapy*

RESUME

Le trouble déficit de l'attention avec ou sans hyperactivité (TDAH) est un trouble neurodéveloppemental fréquent, affectant 2 à 4 % des adultes. Un premier diagnostic à l'âge adulte est fréquent, bien que dans la plupart des cas un TDAH était présent dès l'enfance, mais non identifié ou bien compensé. Le TDAH chez l'adulte s'associe très souvent à d'autres troubles ; les plus fréquemment retrouvés sont les troubles anxieux, les troubles de l'humeur, les troubles de la personnalité, les troubles addictifs, comportementaux et liés à l'usage de substances et les troubles du sommeil. Le retentissement fonctionnel peut être important, par les conséquences académiques, professionnelles, sociales, familiales, ou liées aux comorbidités. Or, la reconnaissance et la prise en charge du TDAH chez l'adulte sont encore peu développées en France, et le trouble reste un sujet de controverse. Cet article vise à proposer un socle de connaissances actualisé, utile aux professionnels francophones amenés à dépister ou prendre en charge des patients adultes avec TDAH. Les caractéristiques et spécificités cliniques du TDAH et de ses comorbidités sont détaillées, permettant de proposer une stratégie diagnostique et d'évaluation globale. Les approches thérapeutiques, psychologiques, rééducatives et médicamenteuses sont présentées ainsi que des lignes de conduites thérapeutiques, notamment en présence de troubles comorbides.

Mots-clés : TDAH de l'adulte, diagnostic, traitement, comorbidité, méthylphénidate, psychothérapie.

Introduction

Attention deficit disorder / hyperactivity (ADHD) among adults is a frequent but under-diagnosed clinical situation and still the subject of debate. Although it was long considered as a disorder of childhood and adolescence, ADHD continues to affect the adult population, with frequent and severe functional impairment.

The recognition of ADHD in adult populations has increased in recent years, and new clinical practices have emerged. France is in a particular position with respect to other European countries, and there are still very few patients identified and managed [1].

Changes are however underway. In France, research and specialised consultations are developing [2]. There are still challenges, in particular concerning access to care. Better training for primary-care physicians and those in general psychiatry is required to identify adult patients with ADHD, and ensure they are adequately cared for.

We propose an update on present knowledge about ADHD in adults, its evaluation and its management, with a particular emphasis on practical clinical and therapeutic considerations for French practitioners. The method consisted in selecting themes deemed relevant for practitioners, via a review of consensus across authors. Then a review of the international literature was conducted for each theme using the PubMed database. Finally the coherence of the results with published reviews and international recommendations was checked.

ADHD from childhood to adulthood.

ADHD is one of the most frequent neurodevelopmental disorders among children, with an estimated world prevalence of 5% [6,7]. Data derived from prospective follow-up of children with ADHD provide evidence of symptom and/or functional persistence into adulthood for 30 to 60% [8-10], which is in line with cross-sectional epidemiological studies, which estimate the prevalence of ADHD among adults to be between 2 and 4% [11-13]. Yet despite this high prevalence, few adults with ADHD receive the appropriate diagnosis and care [14].

Adolescence is a period associated with alterations in the relative predominance of the different elements of the symptom "triad" – inattention, hyperactivity, impulsivity – whereby inattention is often in the fore, hyperactivity more selective and impulsivity more marked. It is a sensitive period characterised by the development of personality, possibly pathological [15], the emergence or exacerbation of mood or anxiety disorders, and a more marked prevalence of externalised disorders such as oppositional defiant disorder, or conduct disorder. Risk-prone behaviours are more frequent (accidents, risk-prone sexual behaviours [16]), and the rate of discontinuation of care is high [17,18].

ADHD clinical characteristics among adults

The clinical manifestations of ADHD among adults involve a triad of symptom, combining to a varying degree inattention, hyperactivity and impulsivity. There are thus three clinical presentations: The predominantly Inattentive presentation, , the predominantly hyperactive/impulsive presentation, and the combined presentation. While this last presentation is generally the most frequent in adulthood, an improvement in hyperactivity/impulsivity symptoms is often observed as years pass. Attention problems for their part persist in more constant manner [24].

It should be noted that ADHD symptoms are variously observed in the population, and that ADHD could be viewed as an extreme manifestation within a symptom spectrum. Unlike most other psychiatric disorders, the diagnosis of ADHD does not rest on the evidencing of a change from a previous state. ADHD symptoms are long-lasting and sometimes subtle, and their functional impact is not always perceived by the patient [25]. This is why family reports and impressions are often essential to make a diagnosis.

Rather than a deficit in the strict sense, most patients appear to present a kind of inability to modulate attentional skills. Some situations can make it difficult to mobilise attention, leading to complaints about difficulty concentrating (reading, meetings, tasks requiring considerable mental effort, conversations). While demanding but not very stimulating tasks are often despised and put off until later (procrastination), adults with ADHD have less difficulty becoming involved in new, stimulating, pleasant activities. Fluctuations in attention are observed, sometimes with a state of hyper-focalisation. Thus a diagnosis of ADHD cannot be denied on the argument that a patient is able, in some circumstances, to concentrate [26]. The same fluctuations are observed for the other inattentive symptoms, such as forgetfulness or blunders. Excessive distractibility is a central symptom, whether the stimulus is external (auditory or visual) or internal. Excessive mind-wandering and daydreaming is a non-specific dimension, but strongly associated with ADHD [26]. Patients report often being overwhelmed by a variety of thoughts, which are non-repetitive, while there is not necessarily any negative emotional valence (such as anxiety disorder), not any relationship with the activity in hand.

In adulthood, hyperactive symptoms often take on a more cognitive form than in childhood, and are often described as jostling ideas that are difficult to control. Motor instability gives way to an excessive urge to move and do things, and to a difficulty relaxing or declining solicitations, or a difficulty in maintaining tact or reserve in situations that require it [26].

Alongside an inhibition deficit, impulsivity in ADHD also takes the form of an aversion to delay. This is particularly observed in the verbal sphere, with a marked tendency to interrupt. Impulsivity can lead to professional problems such as frequent job changes as a result of boredom, as well as problematic relationships or again risk-prone behaviours (speeding, drug use, having trouble with authority).

Beyond the symptom triad mentioned above, other clinical dimensions are found among adults with ADHD. The deficit in executive functioning generates organisational problems

(failure to anticipate, to plan, to hierarchise tasks, or to manage time. Another frequent symptomatic dimension in ADHD is emotional dysregulation. It is characterised by hyper-reactivity, emotional lability, irritability and fits of anger. Any marked presence of these aspects can make differential diagnosis complex, in particular with respect to mood disorders and personality disorders [26].

The symptoms linked to ADHD often force the patient to develop adaptation strategies so as to limit the impact of the symptoms. While these strategies are useful for a large number of subjects, they can take on a dysfunctional appearance, for example with the development of organisational compensations, often costly in terms of cognitive resources, sometimes excessively rigid, making the diagnosis more difficult (compared for example to obsessive functioning).

ADHD has considerable impact on school and professional functioning, and on family and friendly relations. Long-term studies have shown that, in comparison to the general population, adults with ADHD have a lower educational level, lower employment rates, and more unstable familial relationships; they also commit more antisocial acts, and have more accidents, especially at the wheel [27-30].

Diagnostic assessment for ADHD in adulthood

The diagnosis of ADHD in adulthood is based on a clinical approach. The diagnostic criteria commonly used are those of the DSM-5.

The initial assessment comprises three steps (Figure 1). First, a retrospective questioning looks for ADHD symptoms and related impairments before the age of 12, ideally in presence of a family member, and also using school reports. The diagnostic interview then assesses the presence of symptoms of ADHD in the previous six months in order to reach a positive diagnosis of ADHD and its particular clinical presentation. Attention is paid to the assessment of the severity of cardinal and associated symptoms, and the extent of functional impact. Finally, the diagnostic procedure entails the assessment of comorbid medical and psychiatric disorders, so as to weigh up possible differential diagnoses and establish an overall care plan.

Numerous psychometric tools are available to assist the practitioner in this diagnostic procedure (Table 1).

The most widely-used screening tool is the Adult ADHD Self-Report Scale V1.1 (ASRS 1.1.). This self-report questionnaire comprises 18 items based on the diagnostic criteria of the DSM-IV. The first six items form a short version known as the "screener" [31]. This instrument, recommended by the World Health Organization, was recently revised to take account of the DSM 5 criteria [32]. This latest version is at present being validated in French. This assessment is ideally completed with a screening for symptoms in childhood. The Wender Utah Rating Scale (WURS), in particular the short 25-item version, validated in French, provides excellent performances.

The diagnostic assessment generally takes the form of semi-structured interviews. These tools are based on the diagnostic criteria of the international classifications. Among them, only the ADHD Child Evaluation+ (ACE+) and the Diagnostic Interview for ADHD in Adults (DIVA 2.0) [26] have been translated into French. The ACE+ enables the assessment of the disorder using criteria from the ICD-10 and the DSM 5. The DIVA 2.0, more widely used, however, only provides an evaluation based on DSM-IV criteria. The recent version, DIVA-5, using the present DSM criteria, has not yet been translated and validated in French.

Some self-administered questionnaires assess the severity of ADHD, but many of them have no validated French version (Table 1). Others enable the assessment of more specific symptom dimensions of ADHD, such as emotional lability or symptoms of executive deficit. The assessment of the functional impact of ADHD is possible using the Weiss Functional Impairment Rating Scale (WFIRS). It explores the impact of the disorder in numerous areas, and has recently been validated in French [2].

While numerous studies show that adults with ADHD frequently present impairment of executive and attentional functioning, which are measurable using neuropsychological tests, none of these procedures is sufficiently sensitive to establish a diagnosis of ADHD for a given individual, on account of the wide heterogeneity of neuropsychological functioning in this population [34]. These tests can however complete the diagnostic procedure, in particular in order to give insight into indications for cognitive remediation. The same remarks can be made for the relevance of neurophysiological measures such as quantified EEG.

Comorbid conditions in adult ADHD

The majority of adults with ADHD have at least one other comorbid psychiatric disorder [11,35]. The existence of these comorbid disorders makes the diagnostic assessment of ADHD more difficult because some symptoms can be common to both conditions. While numerous psychometric screening tools have been validated in the general population, we would however like to draw clinicians' attention to the risk of over-estimation of these disorders, since there can be an overlap of symptoms across disorders. There is to our knowledge no study assessing the relevance of these screening tools for patients with ADHD, while, alongside, several studies evidence the risk of false positives using the ASRS V.1.1. to screen for ADHD in clinical populations presenting bipolar [36], borderline personality [37] or major depressive disorder (MDD) [38]. A detailed patient history established by the clinician using standardised diagnostic tools should establish the chronology of the onset and the evolution of symptoms of inattention, hyperactivity and impulsivity, and of the onset of comorbid disorders.

The presence of a comorbid condition often requires the therapeutic strategy to be reappraised. Practical considerations for the management of ADHD with comorbidities are presented in Table 2.

Mood and anxiety disorders

Adults with ADHD are more exposed to stressful life events, linked to academic or professional failures and relational difficulties. Self-esteem is often low, partly as a result of the failure to recognise the difficulties experienced. In this setting, MDD is observed for 20% of adults with ADHD [11,39].

The presence of a MDD associated with ADHD has a major impact on global functioning and contributes to a higher suicide risk [39]. Suicidal behaviours, whether completed suicide, suicide attempt, or suicidal ideas, are frequent [40]. Suicidal behaviours are favoured by the presence of an associated mood disorder, impulsivity, alterations in the decision-making process, as well as the intrinsic emotional dysregulation in ADHD.

ADHD is found for 10 to 20% of patients presenting a bipolar disorder [36,41,42]. Conversely, a bipolar disorder is found for around 20% of adults with ADHD [42]. The presence of ADHD affects the characteristics of the bipolar disorder, which is more often type 1, with early onset, more severe and more frequently associated with other psychiatric and addiction disorders [41,43]. Bipolar disorder is also a differential diagnosis in presence of ADHD. These two disorders do indeed share several clinical dimensions, in particular emotional dysregulation and impulsivity [44]. The evolution of symptoms (episodic in bipolar disorder, continuous for ADHD) and the search for symptoms imputable to bipolar disorder alone (insomnia without fatigue or psychotic symptoms over a given period for instance), family history, and response to medication are elements that need to be evaluated to differentiate bipolar disorder from ADHD.

Almost half of the adults with ADHD present comorbid anxiety disorders, that are more severe and with earlier onset [11]. Symptoms of anxiety can be of different types: generalised anxiety, social anxiety, panic disorder and also obsessive symptoms. The presence of these disorders can lead to a delay in the diagnosis of ADHD, because the inhibition often observed among anxious patients can mask the hyperactivity or impulsivity [45].

Addictions and eating disorders

Addictive behaviours are also strongly associated with ADHD, whether in the form of substance use disorders (SUD) or behavioural addictions, in particularly eating disorders. These disorders could be the result of common endophenotypical traits underpinned by a genetic predisposition shared with ADHD [46].

A study in the general population evidenced an increased risk of SUD among subjects presenting symptoms of ADHD, with a relative risk ranging from 1.33 for tobacco use to 3.58 for alcohol dependency [47]. Likewise, other studies found a lifetime prevalence of alcohol abuse for 47% [48] and a current prevalence of alcohol dependence of 21% among subjects with ADHD [49]. Alongside, the prevalence of ADHD among subjects with alcohol dependence is thought to be high, ranging from 23 to 33% of patients receiving care in addiction unit [50].

Adults with ADHD also frequently exhibit cannabis use [51]. This strong association could be explained by the immediate effects of this substance on symptoms of hyperactivity and intolerance towards boredom. This form of "self-medication" is particularly marked among users of stimulant drugs (amphetamines and cocaine), the effect sought being inner calm and enhanced attention [52]. Thus practitioners in addiction centres should be particularly aware of the possibility of ADHD among subjects for whom the substance is used for purposes of cognitive enhancement.

The potential role of stimulant treatments in the genesis of addictive comorbidities in A DHD has long been the subject of debate, including within the medical community. However recent work has not produced any arguments in favour of this association, and it indeed suggests that there is a possible protective effect of pharmacological stimulants [53,54].

Finally, ADHD in adults is also associated with eating disorders, where the mechanisms are close to those of addiction, in particular for bulimia and hyperphagia [55]. Psychostimulants are sometimes used by patients with anorexia. Lisdexamfetamine has recently received marketing authorisation for the indication of binge-eating disorder in the USA [56].

Personality disorders

Between 10 and 75% of adults with ADHD meet criteria for personality disorders [57], the most prominent being cluster B disorders (borderline personality disorder, especially among women, antisocial and narcissistic personality disorders among men), and to a lesser extent cluster C disorders (avoiding and dependent personality disorders). These personality disorders are particularly interwoven with ADHD symptoms, and they are sometimes phenomenologically close. They share the characteristic of a long-term evolution. Several prospective studies have shown that ADHD in childhood has an impact on personality development [58]. It is likely that ADHD leads to the development of dysfunctional relational modes and behaviour patterns, while at the same time altering self-image. There are however studies that suggest a common aetiology, such as traits relating to novelty-seeking [59]. Parenting styles, in a setting of a marked genetic component for this disorder, could also be a determining factor in the development of personality traits [60].

Among patients with a personality disorder, specific treatment of ADHD can boost the efficacy of psychotherapeutic treatments [61].

Other neurodevelopmental disorders

ADHD and autism spectrum disorders (ASD) share vulnerability factors and common pathophysiological mechanisms. Prior to the DSM-5, the diagnosis of ADHD could not be made in presence of an ASD. Yet 58 to 85% of subjects with ASD present symptoms that are compatible with ADHD [62]. The DSM-5 now recognises the possibility of associated diagnoses of ADHD and ASD, also backing up treatment with methylphenidate for comorbid subjects [63].

Specific learning disabilities, such as impairment in reading (dyslexia), in written or spoken expression, in mathematics (dyscalculia) and developmental coordination disorders (dyspraxia) , are particularly frequent among children with ADHD. These disturbances most often persist into adulthood, and can compound the attention difficulties, in particular in the academic and professional fields. The persistence of coordination disorders can sometimes make it difficult or even impossible to obtain a driving licence.

Sleep disorders

Among both children and adults, ADHD is associated with various sleep disorders in 60 to 80% of cases. On account of its impact on daily activity, the presence of a sleep disorder often contributes to aggravating symptom severity in ADHD, and it also favours the occurrence of other comorbid disorders, in particular psychiatric and metabolic disorders.

Insomnia is one of the most frequent sleep-related complaints among adults with ADHD [64]. Insomnia in ADHD is certainly multifactorial, involving alterations in circadian rhythms, poor sleep hygiene, the effect of stimulant treatments, and the contributions of associated anxiety and/or depressive symptoms. In addition, ADHD is associated with intrinsic sleep disorders, in particular restless legs syndrome (RLS) [65]. This is a neurological disorder characterised by the presence of unpleasant sensations in the lower limbs leading to restless movements, favoured by immobility and relieved by movement, mainly occurring in the evening or at night. RLS, linked to an alteration in the intra-cerebral metabolism of iron leading to dopaminergic dysfunction, shares pathophysiological mechanisms with ADHD. In the context of ADHD, the diagnosis of RLS is rarely made, since its symptoms can be confused with motor hyperactivity.

Sleep disorders have an impact on daytime vigilance, and can exacerbate inattention, impulsivity, and hyperactive symptoms, whereby the subject sustains activity to keep awake. Excessive daytime sleepiness (EDS) is observed for 40% of patients [66], with an increased risk of driving accidents. EDS can be linked to the above-mentioned night-time sleep disturbances, however, around 25% of adults with ADHD do in fact present a hypersomnolence disorder, characterised by a increased sleep duration, sleep inertia, and alterations in the quality of daytime vigilance [66]. There is a clinical and symptom overlap between ADHD and narcolepsy or idiopathic hypersomnia. It is therefore not surprising to observe that most pharmacological treatments for ADHD are also used for hypersomnia.

Other medical pathologies associated with ADHD.

Recent research has evidenced a marked increase in mortality risk and a reduction in life expectancy for adults with ADHD [67]. The factors underpinning this excess mortality risk appear to be numerous, involving the risk of accidents, suicidal behaviours, and non-psychiatric medical disorders. The best-documented associations concern obesity, allergic or immune disorders such as asthma or celiac disease, and migraine [68]. Chronic pain has also been linked to ADHD. This alteration of the state of health of patients with ADHD goes hand in hand with increases in health expenditure [69].

Management of ADHD in adults

Care provision for adult ADHD should be multimodal, and based on non-pharmacological interventions and sometimes completed by pharmacological treatment. Two objectives can be defined (Figure 2). The first task is to reduce the functional impairment arising from ADHD and associated disorders. These measures are basically: psycho-education, cognitive-behavioural therapy, and adaptive measures in particular in school and in the workplace. Treatment also aims to directly improve symptoms using either non-pharmacological strategies such as cognitive remediation, or a pharmacological treatment such as methylphenidate. Finally, any comorbid disorders should receive specific care as a priority, since reducing them can lead to an improvement in ADHD symptoms and reduce the functional impairment.

Although there are not yet formalised, harmonised recommendations at European level, several academic societies has published expert consensuses [3]. In France, there are no expert recommendations for the diagnosis and management of ADHD among adults, although the French National Health Authority (HAS) has recently issued recommendations concerning the detection of ADHD among children [70].

Non-pharmacological approaches

Therapies derived from cognitive-behavioural theory applied to adults with ADHD gather on the one hand cognitive-behavioural therapies (CBT) and on the other dialectic behavioural therapies and mindfulness-based therapies. They can be implemented in group and individual settings.

The different structured programs based on these approaches target the optimisation of adaptation strategies to ADHD symptoms [72,72]. The behavioural component aims to improve organisational skills, planning and time management. The cognitive component targets the subject's ability to undertake durable change, problem-solving strategies and methods to overcome procrastination. Other interventions also include components from dialectic therapies and mindfulness, in particular targeting emotional regulation, management of anger and impulsivity, and "letting go".

Several controlled studies have assessed the efficacy of CBTs in adults with ADHD. A Cochrane review in 2018 including 14 randomised controlled trials assessed the effects of these therapies on 700 adults with ADHD, in comparison to specific or non-specific interventions, in some instances in addition to medication [73]. On account of imprecisions, inconsistencies and methodological limitations, the level of proof was considered to be poor to moderate. While these results appear not very convincing, it is important to note that the main judgement criterion for most of these studies was an improvement in symptoms, while these therapies are essentially based on the development of adaptation strategies aiming to limit the functional impairment resulting from the symptoms, and not to reduce the symptoms. Further good-quality clinical trials are needed, using functional measures tailored to the therapeutic aims of these approaches.

Unlike CBTs, the approaches based on attentional remediation, such as the neurofeedback (NFB) and cognitive remediation target not functioning but the neurophysiological and neuropsychological processes underpinning and leading to the symptoms of ADHD.

Cognitive remediation in ADHD is mainly based on training the working memory. Most existing programmes use a computer interface to deliver the cognitive training. One of the most widely studied cognitive remediation tools accessible in France is the COGMED programme. The benefits of cognitive remediation in ADHD for adults are contrasted. While most studies note an improvement in working memory, few studies show efficacy in functional domains. A recent randomised controlled trial noted an improvement in working memory, persisting six months after the intervention, but with no effect on the symptoms of inattention or hyperactivity, nor on daily functioning linked to executive functions [74].

The NFB technique is another attentional remediation strategy based on neurophysiology [75]. It enables the subject to control electro-encephalographic (EEG) parameters linked to attentional abilities. A positive feedback is delivered to the subject in real time when he/she manages to modify the EEG parameters in the desired way. Unlike studies on children, those concerning adults are fairly rare [76]. The first large study among adults shows a reduction in ADHD symptoms, but without demonstrating superiority in relation to placebo or treatment by CBT. Studies are still required to determine the relevance of NFB in this population [77].

Finally, ADHD and its comorbid disorders are linked to altered functioning in school and in the workplace. Special provisions applied in school should be maintained for adults in training. On account of the difficulties in access to jobs and in keeping a job, in France adults with ADHD can claim recognition of their disability via various statuses (French legislation of February 11th 2005).

Pharmacological treatment

Methylphenidate is recommended for children over the age of six, when psychological, educational, social and family interventions are not sufficient. Methylphenidate is the recommended first-line treatment [5,70]. It is a psychostimulant derived from piperidine. It acts by increasing dopaminergic and noradrenergic transmission by inhibition of reuptake in the synapses. The mechanisms are partly distinct from those observed for amphetamines (no direct release of dopamine at therapeutic doses) with which it shares some structural analogies [78]. The mean biological half-life of methylphenidate is two hours. However, various dosage forms are available, with variable absorption profiles, making it possible to obtain variable durations of action.

In France, methylphenidate is available in several dosage forms: 1) immediate release (IR) (RITALINE®), and 2) Extended release (ER) (RITALINE LP®, QUASYM LP®, CONCERTA LP®, methylphenidate MYLAN LP® and MEDIKINET LP®), the shortest duration of effect (2-4 hours) being observed for RITALINE®, while forms with more prolonged release provide a duration of 6-8 hours for MEDIKINET LP® and RITALINE LP® and up to 10-12 hours for CONCERTA LP®. Prescribers should also be aware of the cost of these various dosage forms, varying from one

to three for RITALINE and CONCERTA LP®. The usual dose is 20 to 60 mg per day, once, twice or in some cases three times a day according to the dosage form.

Instatement of this medication for adults falls outside the market authorisation in France. Only the formulations CONCERTA LP® and methylphenidate MYLAN LP® can be prescribed to adults within the indication if the treatment is instated before the age of 18. Immediate release RITALINE® has a received authorisation for adults, not for ADHD but for narcolepsy. Yet methylphenidate is widely prescribed in many countries with robust data in favour of a satisfactory risk/benefit ratio [79]. According to NICE recommendations, methylphenidate is a first-line pharmaceutical treatment for adult ADHD, along with lisdexamfetamine (VYVANSE®) which is not available in France [5]. It should however be noted that some efficacy data concerning methylphenidate remains controversial [80]. As second-line treatment, in case of unfavourable risk/benefit ratio for stimulants, the use of other compounds is possible, such as non-stimulant treatments like atomoxetine - STRATTERA®, available in France with temporary authorisation for use (ATU), and clonidine - CATAPRESSAN®, the only molecule available in France, but without specific indication for ADHD. Other molecules are available in France for other indications and have been investigated for the treatment of ADHD, among which bupropion - ZYBAN®, and modafinil - MODIODAL®, providing contrasted results [81]. Dexamfetamine – ATTENTIN®, is available in France, but solely under a nominative ATU for narcolepsy. Therapeutic developments are expected in the coming years, for instance concerning prolonged-release guanfacine - INTUNIV®, a non-stimulant treatment which was given a favourable opinion in 2017 by the HAS transparency commission for ADHD in children and adolescents, although with a low rating for medical benefit. Other promising molecules are being assessed, such as prolonged-release forms of mazindol [82] or viloxazine.

It is important to recall that no antidepressant, antipsychotic or anxiolytic treatment has an indication for ADHD. These substances, too often prescribed in the context of ADHD, have no beneficial effect on ADHD symptoms and expose patients to side-effects and the risk of misuse.

Given its dopaminergic properties which could lead to misuse, methylphenidate is subject to regulations on the prescription of narcotics. In France, the initial prescription, which can be renewed by the treating physician, is restricted by law to hospital specialists and/or hospital departments specialised in neurology, psychiatry or paediatrics. Methylphenidate is prescribed for a maximum duration of 28 days, renewable monthly by any other physician, who is allowed to adjust the dose according to tolerance and efficacy of the treatment. The prescription should be reviewed and modified if needed at least once a year by the hospital specialist [83].

Prescriptions of methylphenidate requires particular surveillance for potential adverse effects, which are mainly:

1) neuropsychiatric (insomnia, headache, bruxism, irritability, anxiety, motor or verbal tics, mood changes, emotional numbing, mood swings among bipolar patients, occurrence or aggravation of psychotic disorders)

2) cardiovascular (increased heart rate and/or blood pressure, palpitations)

3) cerebro-vascular (arteritis, stroke)

4) metabolic (loss of appetite, weight loss, impact on growth [83].

The prescription of methylphenidate in France is the subject of close surveillance by the French drug agency (ANSM) via pharmacovigilance centres and addiction centres in order to detect misuse and abuse.

French recommendations have been issued concerning the use of methylphenidate among adults in the setting of narcolepsy [84]. A pre-therapy cardiovascular review is recommended only for subjects presenting a personal or family history of cardiovascular disease. Three-monthly surveillance of weight, heart rate and blood pressure, and of the psychological state of the patient by the treating physician is sufficient. There is no need for cardiac ultrasound scan or Holter ECG during methylphenidate treatment, except in case of specific cardiac symptoms. The administration of methylphenidate in pregnancy is not recommended.

Management of comorbid disorders

Comorbidities are more the rule than the exception in ADHD, so that it is essential to detect and treat associated disorders (Table 2).

Insomnia and circadian rhythm disorders can warrant CBT for insomnia, and chrono-biological measures. CBTs are also an important tool in the care of anxiety or mood disorders comorbid with ADHD. Finally, emotional dysregulation linked to borderline personality disorder should be managed using recent innovating approaches involving dialectic and acceptation therapies known as "third wave" CBTs.

Finally, specific precautions should be taken for the prescription of methylphenidate among subjects presenting comorbidities. For instance, methylphenidate in ADHD patients with comorbid bipolar disorder should only be initiated in euthymic periods, when mood stabilizer medication has been prescribed. The use of methylphenidate is not recommended among subjects presenting motor tics or psychotic symptoms. Vigilance is required for its prescription among subjects with anxiety, non-stabilised MDD or an eating disorder.

Conclusion

In the last two decades, major progress has been made in the recognition, care trajectory and management of childhood ADHD in France. This development has however not benefitted adults very markedly, and strong action is required in the coming decades in this area.

1) We advocate an improvement in the screening for and detection of ADHD, in particular in at-risk populations from low socio-educational environments. Training and awareness-raising are required, in particular among primary-care physicians and those working in the area of addiction and in prisons.

2) Specialised consultations in France are still too few and they cannot today respond to the increasing demand for care, linked to the need to pursue treatment in young adulthood for subjects diagnosed in childhood on the one hand, and to new diagnoses made in adulthood on the other. The emergence of specialised teams in the evaluation and diagnosis of ADHD in adults needs to be supported, so that therapeutic decisions can be validated in collegiate manner.

3) The functional impact of disabilities resulting from ADHD need to be more fully recognised so as to provide better accompaniment of adult subjects in training courses and professional activities. Official recognition of the disability, despite the considerable support that this provides, is still not sufficiently solicited nor obtained.

4) If the identification of this disorder among adults is inadequate, the same is true for suitable care provision. Despite recommendations to consider non-pharmacological intervention strategies as the first-line approach to adult ADHD, the realities of clinical practice are quite different. Because of the scarcity of health professionals trained in the specific non-pharmacological approaches, patients are very often only offered a pharmacological treatment, and in the majority of cases off-label. The absence of reimbursement for methylphenidate is a disadvantage for many patients in a precarious financial situation. Newly-diagnosed adults are doubly penalised. In addition to the delay in diagnosis and the absence of suitable care provision at an early stage, many people are deprived of appropriate treatment.

5) Finally, because of the numerous comorbidities, close collaboration is needed between ADHD specialists and adult psychiatry units, addiction centres or sleep disorder units. Setting up an optimised care trajectory for ADHD and comorbidities is a challenge that requires thorough knowledge of the various disorders and communication among professionals.

Conflict of interest

S. W. This author has no conflict of interest to report
O. M. Speaker for Indivior and Shire. Conferences: invitation from Indivior and Shire
A. I. This author has no conflict of interest to report
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S. B. Conferences : invitation from Mensia, Urgo, HAC Pharma and Shire.
N. P. Conferences: invitation from Lundbeck and OpoPharma

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Figures legend

Figure 1 : Principles of initial assessment for ADHD among adults
The first step in the assessment aims to establish a diagnosis of ADHD. On the basis of arguments collected via the screening tools, a detailed interview then seeks to retrospectively identify symptoms that occurred before the age of 12, followed by the occurrence of symptoms in the last 6 months. Determination of the functional impact and the elimination of alternative diagnoses then enable the diagnosis to be established. The second stage consists in characterising the disorder (clinical presentation, severity of the central symptoms, symptoms associates with the ADHD and the degree of disability). Finally, the last stage seeks to identify any associated disorders, psychiatric, addictive and medical, so as to plan for the overall management.

Figure 2: Principles of management of ADHD in adulthood
The management of ADHD first of all adopts a symptom-based approach, which can be non-pharmaceutical or pharmaceutical, targeting the ADHD symptoms observed. A second stage concerns the management of associated disorders. Finally a functional approach aims to reduce the impact of ADHD using behavioural measures, and obtaining recognition of the disability.

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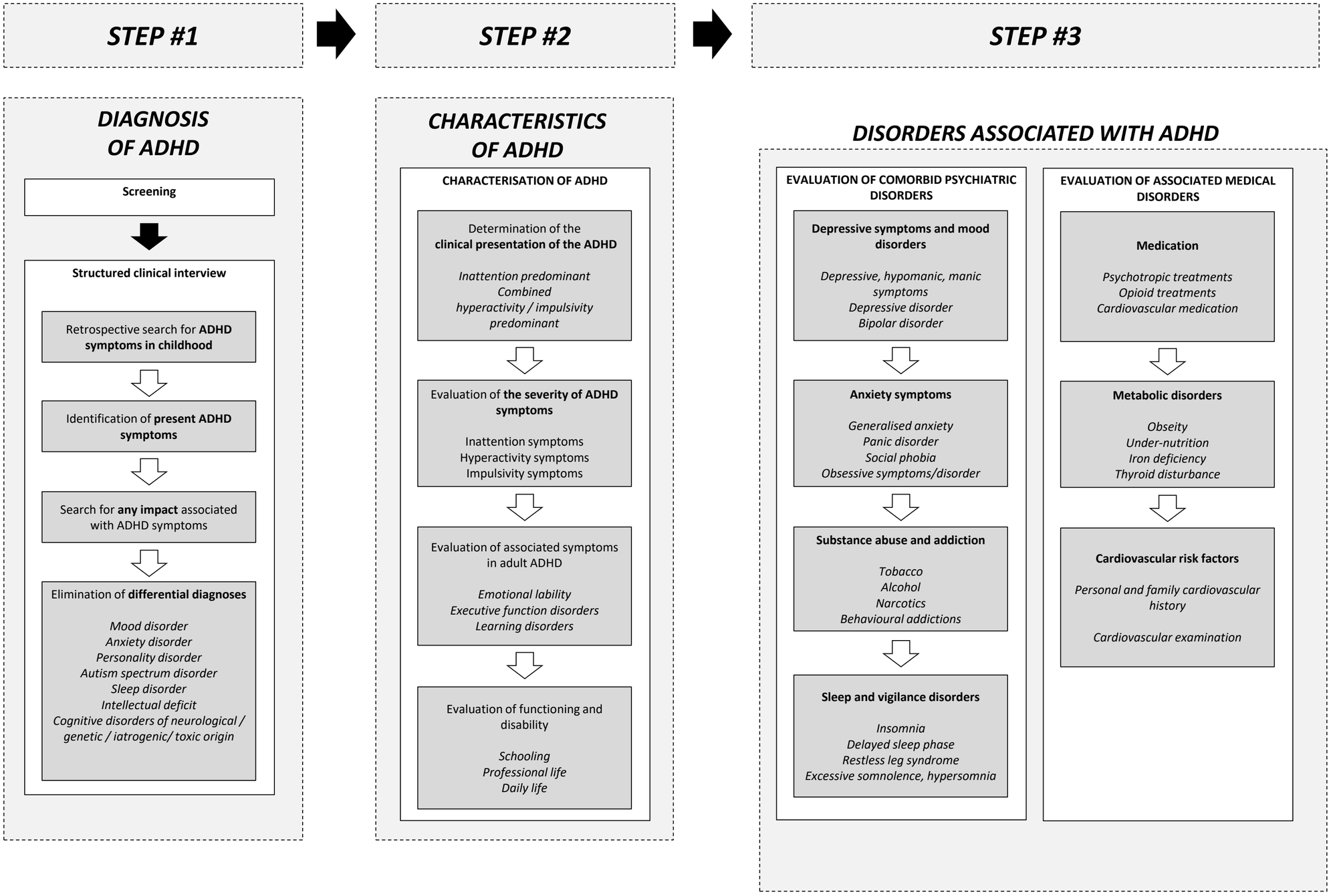
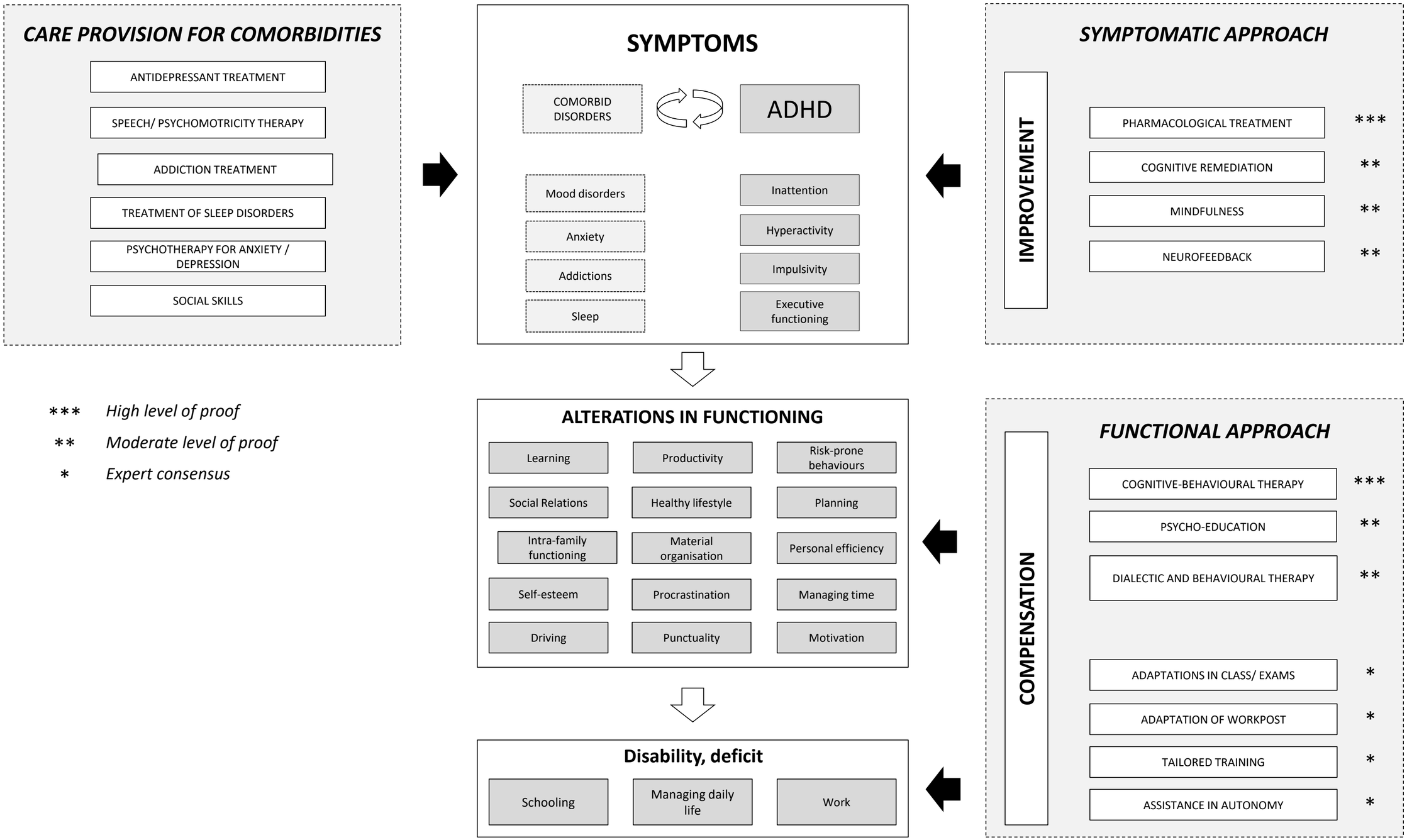

STEP #1
STEP #2
STEP #3
DIAGNOSIS OF ADHD
Screening
Structured clinical interview
Retrospective search for ADHD symptoms in childhood
Identification of present ADHD symptoms
Search for any impact associated with ADHD symptoms
Elimination of differential diagnoses
Mood disorder
Anxiety disorder
Personality disorder
Autism spectrum disorder
Sleep disorder
Intellectual deficit
Cognitive disorders of neurological / genetic / iatrogenic/ toxic origin
CHARACTERISTICS OF ADHD
CHARACTERISATION OF ADHD
Determination of the clinical presentation of the ADHD
Inattention predominant
Combined
hyperactivity / impulsivity predominant
Evaluation of the severity of ADHD symptoms
Inattention symptoms
Hyperactivity symptoms
Impulsivity symptoms
Evaluation of associated symptoms in adult ADHD
Emotional lability
Executive function disorders
Learning disorders
Evaluation of functioning and disability
Schooling
Professional life
Daily life
DISORDERS ASSOCIATED WITH ADHD
EVALUATION OF COMORBID PSYCHIATRIC DISORDERS
Depressive symptoms and mood disorders
Depressive, hypomanic, manic symptoms
Depressive disorder
Bipolar disorder
Anxiety symptoms
Generalised anxiety
Panic disorder
Social phobia
Obsessive symptoms/disorder
Substance abuse and addiction
Tobacco
Alcohol
Narcotics
Behavioural addictions
Sleep and vigilance disorders
Insomnia
Delayed sleep phase
Restless leg syndrome
Excessive somnolence, hypersomnia
EVALUATION OF ASSOCIATED MEDICAL DISORDERS
Medication
Psychotropic treatments
Opioid treatments
Cardiovascular medication
Metabolic disorders
Obseity
Under-nutrition
Iron deficiency
Thyroid disturbance
Cardiovascular risk factors
Personal and family cardiovascular history
Cardiovascular examination



*** *High level of proof*

** *Moderate level of proof*

* *Expert consensus*

Table 1 : Useful tools for the assessment of ADHD in adulthood

Measures	Dimensions studied	Psychometric validation	Mode of assessment	Number of items	Remarks
WURS	Inattention Behavioural disorders Emotional problems	Translated and validated in French	Self-assessment	61 - 25	Retrospective assessment of symptoms in childhood. Two versions available, but the 25-item should be preferred. A score ≥ 36 has sensitivity and specificity of 96%; a score ≥ 46 correctly identifies 86% of ADHD and 99% of healthy subjects [33].
ASRS screener	Inattention Hyperactivity/ Impulsiveness	Translated and validated in French.	Self-assessment	6	Positive if ≥ 4 items positive (grey zone) out of 6. According to Kessler [31], the intrinsic characteristics of the ASRS Screener are better than those of the ASRS-18
ASRS-18	Inattention Hyperactivity Impulsiveness	Translated and validated in French	Self-assessment	18	Threshold 24/36 for each dimension (Inattention et Hyperactivity/ impulsiveness) points to ADHD. [31]
ASRS-5	Inattention, Hyperactivity/Impulsiveness, executive functions	Only translated into French	Self-assessment	6	Version derived from DSM-5 symptoms and symptoms associated with ADHD, including difficulties linked to dysexecutive disorder.. [32]
CAARS	Inattention Hyperactivity Impulsiveness/ Emotional lability Self-esteem	Only translated into French	Self-assessment and observer	26 - 66	Different versions (long or short, scored by patient or family. Each sub-score obtained is interpreted according to gender and age of the patient. Sensitive but not very specific.
WRAADDS	Inattention / Disorganisation Hyperactivity / Impulsiveness / Emotional dysregulation / Temperament / Opposition / Impact	Only translated into French	Hetero- and self-assessment versions	71	Scale assessing numerous symptom dimensions (Utah criteria) not taken into account in the DSM criteria [85]
DIVA 2.0	Inattention Hyperactivity/ impulsiveness	Only translated into French	Hetero-assessment	18	Semi-structured interview based on DSM-IV. A version based on DSM-5 is in preparation The presence (after 17 years) of 5 out of 9 symptoms for inattention and 5 out of 9 for hyperactivity/impulsiveness is in favour of the diagnosis.
ACE +	Inattention Hyperactivity/ impulsiveness	Only translated into French.	Hetero-assessment		Semi-structured interview based in 1CD-10 and DSM-5

WFIRS	Assessment of impact : Family, Professional, Schooling, Aptitudes in daily life, Self-esteem, Social functioning, Risky behaviours	Translated and validated in French.	Self-assessment	69	Scale measuring the impact of ADHD in seven main areas of life. Scores can be calculated for each domain with proposals of thresholds for problematic levels [2]
AAQoL	Quality of life : 4 domains : Productivity in daily life, Psychological health, Relationships and View of life	Only translated into French	Self-Assessment	29	Quality of life scale covering difficulties resulting from ADHD [86]
ALS	Emotional dysregulation	Translated and validated in French (in particular on subjects with ADHD).	Self-assessment	18	Quantitative scale for emotional dysregulation; no pathological threshold defined. [87]

Abbreviations : AAQoL, Adult ADHD Quality Of Life; ALS, Affective Lability Scal ; ACE+, ADHD Child Evaluation +; ASRS, Adult ADHD Self-Report Scale; CAARS, Conners Adult ADHD rating Scales; DIVA 2.0, Diagnostic Interview for ADHD in Adults; WFIRS, Weiss Functional Impairment Rating Scale; WRAADDS, Wender-Reimherr Adult Attention Deficit Disorder Scal ; WURS, Wender Utah Rating Scale

Table 2 : Practical considerations for the management of ADHD and comorbid disorders

Associated disorders	Considerations for management
Depressive disorder	• A depressive episode requires optimal care before starting management of ADHD • Non sedative and non-tricyclic antidepressants should be preferred (e.g. noradrenergic antidepressants)
Bipolar disorder	• There is a risk of mood swings under methylphenidate, but the effect is lesser than with antidepressants • Methylphenidate can be prescribed after a return to euthymia, and in association with a mood stabilizer • Mildly sedative, non-antipsychotic mood stabilizers should be preferred (e.g. lamotrigine, lithium)
Personality disorder	• The psychotherapeutic treatment of personality disorders is more efficient if the associated ADHD is treated • Impulsivity, particularly in borderline personality disorder, can be improved by treating associated ADHD • Methylphenidate treatment can be envisaged after taking account of disorders linked to substance use, which are frequent in personality disorders.
Anxiety disorders	• The prescription of methylphenidate should be envisaged with caution when a non-stabilised anxiety disorder is associated, on account of the risk of exacerbating symptoms via the stimulant and sympathomimetic properties of this molecule • Atomoxetine or clonidine can be an alternative to methylphenidate in this situation. • Benzodiazepines can aggravate attentional disturbances and increase sedation
Substance-use disorders	• The prescription of methylphenidate is possible in presence of an associated substance-use disorder, with particular surveillance • Prolonged-release forms rather than immediate release forms should be preferred. • CONCERTA® dosage form and its method of delivery via osmotic pump makes it more difficult to misuse than capsule preparations • Clonidine is an option that can be envisaged in cases where the misuse of methylphenidate appears likely. • Methylphenidate can be accompanied by an increase in craving and substance use, in particular tobacco. • Bupropion is a therapeutic option to be envisaged for tobacco cessation among adults with ADHD
Eating disorders	• The prescription of methylphenidate should be envisaged with caution in the setting of eating disorders, on account of the anorectic effects of the molecule • Non-stimulant molecules such as atomoxetine or clonidine can provide alternatives.
Insomnia	• Methylphenidate can cause insomnia. It is preferable to use short-release forms, with intake distant from bedtime • Insomnia in ADHD should first be managed in a cognitive behavioural approach. Low-dose clonidine at bedtime can be envisaged if this fails
Circadian rhythm disorders	• Chronobiological treatments can be envisaged, in particular imposing early morning rise, limitation of light exposure at bedtime and light therapy on waking. • Compounding preparations of melatonin can be envisaged, to be taken at a fixed time in the early evening
Restless legs syndrome	• The presence of RLS should motivate screening for associated iron deficiency, requiring supplementation for ferritin levels below 50ng/ml • The prescription of a dopaminergic agonist is possible in presence of RLS among adults with ADHD
Hypersomnolence	• The presence of excessive daytime sleepiness, in particular in overweight subjects, should motivate screening for sleep disordered breathing. • Modafinil can provide an alternative to methylphenidate in case of hypersomnia with ADHD.