

Treatment of adult ADHD: a clinical perspective

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Ther Adv Psychopharmacol
2018, Vol. 8(1) 25–32
DOI: 10.1177/
2045125317734977
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Abstract: Adult attention deficit/hyperactivity disorder (ADHD) has moved from the blurred edge of clinical focus to clear recognition as a prevalent and significant disorder in its own right. It is a relatively common comorbidity which if identified and treated may open the door to better outcomes for hard-to-treat patients. Conversely, failure to identify and treat adult ADHD is linked to negative outcomes. The recognition of the importance of adult ADHD in a subset of our patients challenges us to overcome our anxiety about this diagnosis and prevent the societal marginalization of vulnerable patients. Adult ADHD responds well to integrated pharmacological and psychotherapeutic intervention. Its treatment responsiveness reduces disability and allows the comorbidity which is typically present to be addressed. Mastering this challenge can make the diagnosis and treatment of adult ADHD a rewarding experience.

Keywords: Adult ADHD, ADHD, treatment, stimulant, non-stimulant, non-pharmacological, co-morbid

Received: 1 June 2017; revised manuscript accepted: 21 August 2017.

The social and medical context of adult ADHD

Like many psychiatrists, we began our medical and psychiatric training in the last century. We were taught that patients with adult attention deficit/hyperactivity disorder (ADHD) had a dubious diagnosis and were probably seeking stimulants for nefarious purposes. Doctors working in this field were viewed with suspicion. They were regarded either as gullible, permissive clinicians or, worse, unscrupulous suppliers of stimulants to drug seekers.

The long-held belief that persistence of childhood disorder into adulthood was rare has been challenged by the remarkably consistent finding that ADHD frequently persists into adulthood^{1–3} and although childhood evidence of ADHD is required for formal diagnosis, it is possible that a variant may have an adult onset.^{4,5} Prejudices about adult ADHD have been confronted by the recognition of its presence in psychiatric settings. As clinicians who have spanned this transition, we are grateful to the editors for their invitation to put forward a clinician's perspective on managing adult ADHD.

As evidence of neuropathology⁶ and variable degrees of cognitive impairment^{7–10} in adult

ADHD has mounted, new generations of psychiatrists have entered practice and new perspectives have emerged. Cognitive functioning, and in particular executive system function, has become central to our understanding of disability in psychiatric illness. The primacy of this facet of human performance in the lives of our patients means cognitive function has become a key complaint for many disorders. Limitations in this domain have profound consequences for all the important requisites of wellbeing: education, work mastery, relationship success and conflict resolution. Cognitive dysfunction is often a rate-limiting step in converting hours in therapy to the attainment of a connected and productive life. There is marked heterogeneity in the cognitive profiles of adults with ADHD, with neuropsychological tests suggesting that about 11% do not have measurable cognitive dysfunction (higher IQ and medication were noted to convey some degree of protection). However, those with more marked executive dysfunction, working memory difficulty and/or impulsivity tended to show the greatest degree of impairment in daily functioning.^{7–10}

The legitimacy and clinical importance of adult ADHD are still challenged in the lay press by an amalgam of conservative medical traditionalists

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who demand psychiatry provides the pseudo-certainty of biomarkers and an anti-medicine group concerned about their perceptions of pharmaceutical industry influence.

In the face of this resistance to ADHD as a diagnosis, evidence of the validity and clinical relevance of adult ADHD has accumulated. Adult ADHD genetics reveals heritability estimates of around 70%. Earlier estimates had suggested lower heritability than childhood ADHD, but improved methodology showed them to be similar.^{11–14} The epidemiology suggests adult ADHD is underdiagnosed – conservative adult population prevalence is 2.5%.^{2,15} The psychiatric comorbidity levels are high – 60–70% of adults with ADHD have a comorbid disorder.¹⁶ ADHD is even associated with medical comorbidity, with an increased risk of obesity, sleep disorders and asthma.¹⁷

The potential consequences of untreated ADHD have been shown in many recent studies, some examining the long-term outcome of childhood ADHD and others exclusively examining adult ADHD. They include:

- (1) impaired quality of life;¹⁸
- (2) impaired relationships;^{19,20}
- (3) reduced employment;^{21,22}
- (4) vulnerability to addiction;^{21,23}
- (5) vulnerability to depression and anxiety;^{21,24–26}
- (6) impaired driving safety;²⁷
- (7) premature death from accidents;²⁸
- (8) suicide.^{29,30}

Psychiatry leads societal efforts to reduce the deep, historical stigmatization of mental illness. Undoubtedly there have been great inroads here against the large targets, such as major depression and anxiety disorders. ADHD suffers from the familiar mindset that major depression and post-traumatic stress disorder have endured, where symptoms on a continuum of normal experience lead to accusations of medicalization: ‘everyone loses concentration’, ‘we all get distracted and forget things’. There is a resistance to perceiving ADHD as a disabling disorder in part because of this question about the spectrum of normality. Yet medical disorders including asthma, hypertension, type 2 diabetes, sleep apnoea and obesity all exist on spectra. Continuum issues are not unique to psychiatry. In fact, they are the norm in first-world medicine where chronic condition

management is the main task of the medical practitioner. Like other conditions, we have guidelines to the thresholds that help us distinguish normal from abnormal, and a growing body of emergent research into ADHD provides a clearer demarcation of ADHD as a syndrome.

What the research demonstrates with great clarity is that adult ADHD is more prevalent than we thought;^{2,3,6} it is often missed and is likely to be found as a comorbid disorder.^{16,21,23–26} Adult ADHD is associated with impaired quality of life,^{18–20} persistent morbidity^{22–25} and elevated mortality risk.^{28–30} In psychiatry, stigma, complexity and occasional controversy are familiar foes. Our role is to thoughtfully discern disorder through diagnostic complexity, and advocate for those living with hidden disability. We have to use our skills to identify and treat adult ADHD, yet remain critical enough to keep diagnostic thresholds meaningful.

Diagnosis

The usual journey to diagnosis of adult ADHD is one of false starts, alternative diagnoses and the patient’s own perception of continuing cognitive dysfunction despite engaging with psychiatry. Typically patients with ADHD will have seen other doctors and made attempts at seeking treatment – often for depression, substance-use disorders (SUDs) or anxiety. Many ADHD patients have discovered their own laborious ‘work-arounds’ in their attempts to perform at university and at work. The characteristic that often strikes the clinician is how hard the patient has worked for many years to counteract their lack of attention and poor concentration. The ‘quick and easy one stop diagnosis and script’ is, in our experience, a prejudicial myth.

The clinical diagnosis of adult ADHD is complex and deserves an article in its own right. ADHD symptoms are most evident in a world of competing attentional demands. An interview in a medical office will typically elicit a history of symptoms and accumulated life consequences of ADHD rather than any objective signs beyond mild restlessness. Typically patients or their spouses complain of occupational difficulty (being subject to disciplinary processes, losing jobs, educational dropout), disorganization (time management problems, personal and financial administrative difficulty) and proneness to procrastination.^{20–22} Becoming overwhelmed and distracted are common problems for people with ADHD, who may

commence many tasks but struggle with task completion. Anxiety, insomnia and a demoralized and self-deprecatory presentation of depression often accompany this picture.^{16,18,19} Impulsiveness means comorbid SUDs^{16,23–26} and binge eating¹⁷ are frequently problematic.

We do not have to leave our office or even declare a professional interest to see ADHD. Careful screening of eight European countries' adult psychiatric clinic populations using a World Health Organization validated rating scale (ASRS v1.1) and a structured diagnostic interview (DIVA 2.0) identified ADHD in 15.8% of this population (9–30.8%). In this mixture of private and public clinics a majority of those found to have adult ADHD were attending to treat another disorder. In fact, 53.9% had never been diagnosed with ADHD, and two-thirds had never had treatment for ADHD. An overwhelming 88.5% had another diagnosis.³¹ As clinicians we value both of the freely available instruments used in this study in diagnostic assessment, but note that clinical diagnosis is aided, rather than defined by, rating scales.

Although at times investigations are helpful in assessment, there are no pathognomic neuropsychology or neuroradiology findings. Instead, diagnosis requires detailed assessment (usually over multiple interviews) and clinical judgement. It includes a thorough history and longitudinal evidence of ADHD beginning before 12 years of age (preferably from collateral sources such as school records, childhood health assessments and family observations). As a continuous rather than episodic disorder it also requires a pervasive, and enduring pattern of difficulties that impair social functioning and limit the realization of potential. Medical examination is usually unremarkable. However, elevated rates of neurological disorders such as Tourette's syndrome, epilepsy and cerebral palsy, and associations with poor nutrition and SUDs, should all be considered in medical examination. Weight and cardiovascular fitness (especially blood pressure) are important baselines as ADHD treatments may either improve or worsen these parameters. Although cardiovascular safety is good for ADHD treatment, one still has to screen for ischaemia or a family history of arrhythmia that could preclude stimulant treatments.

Management

Available ADHD treatments have impressive effect sizes³² and the improvement that can be

achieved in both ADHD and previously intractable comorbid conditions is rewarding for both patients and therapists. Frequently impaired inhibition brings a disarming openness which may be endearing. This can be an important redemptive quality for a well-meaning, but error prone, individual. However, there are challenges in treating patients who are to varying degrees impulsive, disorganized, and distractible, especially as they may also be prone to procrastinating and forgetting appointments.

In ADHD, aberrant neurophysiology drives cognitive style and patients will attend to things that are both immediate and personally salient. They will shift rapidly if another issue becomes salient to them or struggle to shift with the therapist if the subject is perceived as minor or only of importance to the therapist. Therapists need to overtly establish each patient's goals and relate treatment to them. They need to advocate strongly for therapeutic targets (like motivational interviewing, this often involves emphasizing personal reward and/or cost).

Therapists need to be flexible, engaging and direct. In contrast to the neutrality required in some psychotherapy, humour and demonstrativeness are essential therapeutic tools. These patients need affective engagement and appreciate bluntness. Impaired memory and executive function mean instructions and appointments should be emailed or entered directly in a diary (preferably in a phone with two audible alerts for the pending task). If clinicians let paper leave the office they should not expect to see it again. To track progress, we suggest using rating scales such as the Adult ADHD Symptom Rating Scale (ASRS v1.1) in the office.^{33,34} Sending written information/instructions electronically ensures your treatment plan is not left behind or lost on the way to the car.

Complex regimens dramatically reduce treatment adherence. With a syndrome like ADHD, in which cognitive dysfunction is common, it is absolutely essential that treatment is simple and structured. Connection to daily routines and in-built reminders help (mobile phone apps with audible alerts are again useful).

Psychosocial treatment

We advocate for combined pharmacotherapy and psychosocial treatment and disagree with

relegating pharmacotherapy to a secondary status. No one treatment is any more moral than another. It would be an unusual respiratory physician who prioritized physiotherapy over inhaled bronchodilators/corticosteroids in managing asthma. Improving cognition pharmacologically enhances the engagement with psychosocial interventions in both ADHD and comorbid disorders.

Non-pharmacological therapies including condition-specific psycho-education for patients and families,³⁵ ADHD-tailored CBT (typically these build skills and routines focused on organization, prioritization and time management while challenging self-defeating cognitions),^{36–39} ADHD coaching⁴⁰ and exercise^{41,42} have each been shown to provide some benefit. They may overcome procrastination and provide complementary improvements in executive functioning by utilizing training in organization and time management skills. There is good evidence for the success of these therapies alone or in addition to pharmacotherapy. They can be delivered by psychiatrists, psychologists or ADHD coaches. In clinical practice, maximum yield and therapeutic efficiency is obtained when psychosocial interventions are delivered in addition to pharmacotherapy as a part of multimodal treatment.^{43–46}

Stimulant therapies

Stimulants are first-line pharmacologic agents for adult ADHD with a long history and moderate to large effect.^{32,47} Like all treatments, side-effects occur (reduced appetite and initial insomnia during initiation especially), but tolerability and overall safety are good, especially when compared to most psychiatric medicines. Safety improves further when their beneficial effects on driving are factored into the equation.^{48,49} Cardiac safety is established with no increase in serious cardiac illness. Underlying cardiac vulnerability and a small increase in blood pressure (around 2 mm Hg once stable) need to be considered. Starting low but titrating rapidly towards target dosing is recommended to avoid frustration in this inherently impatient group.⁵⁰

Long-acting formulations allow once-daily simple treatment regimens so in the real world they are more effective than short-acting preparations and less prone to abuse/diversion. Their pharmacokinetic profiles reduce profound onset and offset effects that can either disturb patients or occasionally foster misuse. They lack flexibility, but

reliable, stable patients can augment these by ‘topping up’ their dose with a small amount of short-acting formulation if they are required to do evening driving, study or work. It should be noted that recognition of ADHD in adulthood is a more recent phenomenon. This means that compared to childhood ADHD, we have less evidence on the long-term outcome of pharmacological treatment in adult populations, particularly for those in middle age and beyond.

Less explored than classical stimulant therapies based on methylphenidate and dexamphetamine is modafinil.^{51,52} Although not regulated in the same way as classical stimulants, modafinil shares many pharmacological properties. Once a mystery, its mechanism of action is now understood to be at least in part dopamine reuptake inhibition. A small but positive literature supports its clinical utility as an alternative to traditional stimulants; however, it should be noted that its use for ADHD is ‘off label’ in many places.

Growth is hardly a concern for adult ADHD, and drug holidays are a largely discredited concept, so we advocate daily dosing across 10–14 h rather than excessive focus on use during work or study times. The evidence on quality of life, family relationships and social dysfunction argues against seeing ADHD as primarily an occupational impairment. Like other psychiatric disorders, ameliorating ADHD is primarily to benefit our patients and their families. Benefit to employers flows on from improving patients’ functioning and employment stability, rather than being a primary goal.

Controlled drugs entail pharmaco-vigilance, but evidence suggests they may reduce rather than increase the risk of substance abuse. Most patients use medication responsibly and their improved executive function and reduced impulsivity often reduces misuse of alcohol and illicit drugs.

Bipolar and SUD populations have high rates of ADHD and provide therapeutic challenges. Bipolar patients can safely use stimulants but only with mood stabilization in place, cautious dosing and close monitoring.^{53,54} In SUD patients there is a limited evidence base on treating ADHD, but the recent evidence favours robust stimulant dosing.⁵⁵ This obviously provides a clinical conundrum. Secure slow-release formulations with tight prescribing and dispensing controls are needed as the group most prone to misusing short-acting

stimulant therapy are adults with pre-existing SUD. This is analogous to the established and effective strategy of opioid replacement with the added bonus of directly improved executive system function. This cognitive improvement may enhance decision-making and adherence to SUD treatment protocols.

Non-stimulant therapies

Non-stimulant therapies are typically second-line pharmacotherapy for adult ADHD. They may be used as

- (1) monotherapy in patients not suited to stimulant therapy;
- (2) augmenting treatment in combination with stimulants;
- (3) treatment for comorbid depression and/or anxiety where thoughtful prescribing allows for additional direct treatment of ADHD symptoms.

Although the effect size on ADHD symptoms is typically not as robust, they offer around-the-clock benefit, have less stigma, fewer regulatory controls and less potential for diversion. The best studied non-stimulant pharmacotherapy is atomoxetine.^{32,56,57} Selected antidepressants have a much smaller evidence base, but may provide a similar benefit (TCAs,⁵⁸ bupropion,^{59–61} SNRIs and agomelatine^{62,63}). The unifying theme among these medications is their promotion of noradrenergic and/or dopaminergic actions in prefrontal cortex. This fits with our understanding of the pathophysiology of ADHD and mirrors the known effects of stimulant medications.

Alpha 2 adrenergic agonists clonidine and guanfacine have some evidence of benefit in adult ADHD.³² The effect sizes are small and they can cause hypotension, so they are really only occasionally used as adjuncts. Like melatonin,⁶⁴ they are used primarily for addressing ADHD-related sleep disturbance, where they are more clearly beneficial.

Other therapies

Cognitive training⁶⁵ and neurofeedback^{66,67} are enticing; however, more stringent studies suggest their effect is smaller than commercial claims would have us believe. Tempting morsels on the pro-cognitive effects of tDCS⁶⁸ and rTMS⁶⁹ are interesting but not yet of clinical relevance to adult ADHD.

Restrictive diets simply do not work in adult ADHD, and extravagant claims from alternative health marketing lack scientific credibility or evidence of efficacy. In short, they are baseless quackery.

Conclusion

The impact of cognitive dysfunction across a range of psychiatric disorders is a key predictor of disability and a growing focus of treatment. Adult ADHD is a prevalent but under-recognized disorder in psychiatry, frequently with a cognitive syndrome as a prominent feature. Research consistently shows high prevalence, strong heritability and high comorbidity with unequivocally serious mental and physical conditions. Comorbidity data on adult ADHD creates a different view of the psychiatric waiting room than existed before it became a mainstream diagnostic entity.

Cutting through diagnostic uncertainty, and seeing beyond the stereotype of adult ADHD being the legitimizing mask substance abusers wear to gain access to stimulants, allows a different view – one in which adult ADHD is considered a disabling, and yet treatment-responsive, disorder. Successful treatment improves patients' quality of life.

If we overcome our anxiety about a disorder in which both the illness and its treatment are stigmatized, we can address the elephant in the waiting room by identifying and treating adult ADHD. Psychiatrists do not need to specialize in adult ADHD, simply addressing what is a prevalent comorbidity in our patients offers a chance to reduce disability and enable improved treatment of depression, anxiety and SUD. Clinical experience suggests treating comorbid adult ADHD in select patients may be a key to treating a common matrix of comorbidities: depression, anxiety and SUD. In this group these hard-to-treat problems may become more amenable to directed treatment if the disability of ADHD can be mitigated. Addressing adult ADHD provides an opportunity to reverse demoralization and open up doors to effective functioning for a subset of our patients who hitherto have struggled to implement the treatments we recommend.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest statement

This invited article is from clinicians with a specialty interest in adult ADHD. We believe our Australian urban practice is typical of first-world experience in this evolving field. Although the views expressed are entirely personal, they are informed by evidence, expert opinion and clinical experience.

Dr Geffen declares no current conflicts. He has received payment for advisory board membership (Pfizer) and educational speaker fees (Servier, Lilly, Janssen, Organon, Lundbeck, Shire, Pfizer, Astra Zeneca).

Dr Forster declares no competing interests.

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