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ADHD and Mood Disorders in Adulthood: Diagnostic and Management Issues Confronting the Clinician - June 2010



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Professor Schweitzer has participated in intensive investigations of the biological aspects of depressive disorder, including neuroendocrine and neuroimaging studies. A great deal of his research has focused on the psychopharmacology of mood and anxiety disorders, as well as schizophrenia.

He has been the recipient of many major research grants and has been awarded NHMRC funding to pursue studies in ECT. He has been on the editorial board of several journals and is a former Vice President of the World Federation of Societies of Biological Psychiatry.

About Research Review

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A Research Review Speaker Series is a summary of a speaking engagement by a major local or international expert and allows it to be made available to a wider audience through the Research Review membership or physical distribution.

Research Review publications are intended for New Zealand medical professionals.

This publication is a summary of a recent presentation by Professor Isaac Schweitzer, Medical Director, The Melbourne Clinic, Healthscope Chair of Psychiatry, University of Melbourne. He addressed child, adolescent and adult psychiatrists, paediatricians, nurses and psychologists, in New Zealand in June 2010 about ADHD and mood disorders in adults, focusing upon the diagnostic and management issues that confront clinicians.

Adult aspects of ADHD: abundant controversy

As Director of the Mood Disorders Unit at The Melbourne Clinic, Australia's largest private psychiatric hospital, Professor Schweitzer's interest in attention-deficit hyperactivity disorder (ADHD) in adulthood has developed over the last 5–10 years in response to tertiary patient referrals. The majority of patients referred to him and his unit, and other such mood disorders units, comprise patients with treatment-resistant mood disorders. One of the most important reasons for treatment-resistant disorder is either misdiagnosis or the presence of an undiagnosed and untreated co-morbidity, such as bipolar disorder, personality disorder and substance abuse. Professor Schweitzer and his colleagues have become increasingly aware that a significant proportion of their adult patients with treatment-resistant disorders have an underlying ADHD.

Much controversy surrounds the concept of ADHD in adulthood. The diagnosis (see textbox) is viewed by many in the medical profession and in the wider public with considerable scepticism, as epitomised by a polarised debate published recently in the *BMJ*. Psychiatrist Philip Asherson and colleagues argue that the concept of ADHD in adults is valid, a disorder in which the effects of stimulants and atomoxetine on ADHD symptoms are similar to those seen in children.¹ In contrast, psychiatrists Joanna Moncrieff and Sami Timimi state that the diagnosis is supported by little more than aggressive marketing by pharmaceutical companies, eager to profit from the expanding and lucrative market for stimulants and related drugs.² They contend that more robust evidence is required before we can accept a concept such as adult ADHD, which departs from established views of the nature of behavioural problems, has high comorbidity with more established diagnoses such as various personality disorders, depression, anxiety, and bipolar disorder, and can only be tenuously linked to the childhood disorder. In their opinion, ADHD in adulthood is simply the latest of several medical and psychiatric fashions, which have been fuelled by the interests of the drugs industry.

Controversial issues to consider

Professor Schweitzer speculates that ADHD in adulthood is probably the most controversial of diagnoses in psychiatry today. He advises that our discussions, both formal and informal, should be considering several controversial issues, as outlined below:

- Does ADHD persist in to adulthood?
- Is ADHD in adults a 'medicalisation' of a normal variation of human behaviour?
- Is ADHD over diagnosed and over treated?
- Is it possible to distinguish ADHD in adults from major depression, bipolar disorder, personality disorder and anxiety disorder?
- Is treatment of ADHD in adults worth the risks?

ADHD in adults is almost always a continuation of ADHD from childhood. Professor Schweitzer therefore prefers the term "ADHD in adults", as opposed to "adult ADHD", which tends to suggest that the disorder may first appear in adulthood. Only in the last decade has it been understood that children do not really grow out of ADHD upon reaching adulthood.

Some would argue that ADHD in adults is a medicalisation of a normal variation of human behaviour; similar criticism has been levelled at many other established psychiatric disorders.

We currently lack sufficient evidence to be certain as to whether ADHD in adults is over- or undertreated. Professor Schweitzer suspects that the disorder is underdiagnosed and undertreated in most parts of the world.

It can be difficult, even for the experts, to distinguish ADHD from other major psychiatric disorders.

The cardiovascular risks of stimulant drugs used to treat ADHD are well recognised. In 2006, the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration (FDA) voted to recommend a black-box warning describing these risks, which include myocardial infarction, stroke, and sudden death in children and adults taking ADHD stimulants.³ Substance abuse has also been well characterised in regard to stimulants, abused for both "performance enhancement" and recreational purposes (i.e., to get high).⁴ Stimulants have been specifically used to enhance performance by suppressing appetite (to facilitate weight loss), increasing wakefulness, and increasing focus and attention.⁴

ADHD is a clinical syndrome defined in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, by high levels of hyperactive, impulsive, and inattentive behaviours in early childhood that persist over time, pervade across situations, and lead to notable impairments.

Case vignette – the impact of ADHD on marriage

ADHD can lead to conflict and high levels of distress in marriage. Professor Schweitzer discussed details of a case that may be considered typical of many adults presenting with ADHD who were not diagnosed as children.

This 39-year-old man was referred by his general practitioner for assessment and management advice of bipolar disorder. His pregnant wife, who was also his business partner, had become increasingly frustrated with him as he persistently failed to follow through on tasks, such as the banking, shopping and other chores, attending appointments.

He would often be irritable, overbearing and verbally but not physically aggressive. He was forgetful, described his thoughts as 'scattered', would often lose things and became easily distracted. He was fidgety, found it hard to sit still for extended periods, and needed to be on the go. He would interrupt people and intrude on conversations.

He recalled his difficulties stemming from childhood, as far back as he could remember. He had always been told he had a learning disability and found it difficult to study. At school he was an excellent sportsman, popular with peers, but poor academically.

At school, he was fidgety, easily distracted and had poor concentration and attention span. He left school after failing to pass Grade 10.

He had run in to difficulties in past relationships. He admitted to having taken amphetamines in the past; this he felt improved his concentration. Many years earlier he had experimented with ecstasy. He has had two drink driving charges and has had several speeding offences.

Previous psychiatrists had told him he had bipolar spectrum disorder and treated him with valproate and antidepressants. Others had told him he had an anxiety disorder. Previous treatments did not help.

His wife and mother both confirmed his lifelong history with this disorder.

Provisional diagnosis:

- ADHD
- Past substance abuse
- Narcissistic and dependent personality traits.

Initial treatment with atomoxetine proved very helpful, but caused severe nausea. He is now receiving methylphenidate.

ADHD: some facts

ADHD is well established in childhood. The British Child and Mental Health Survey in 1999 established that 3.6% of children aged 5–15 years are affected by ADHD.⁵ In the United States, ADHD is diagnosed in an estimated 8% of children aged 4–17 years and in 2.9–4.4% of adults.^{6–8} Similarly, 7.9% (12.3% males and 3.8% females) of Australian youth aged 12–17 years have been diagnosed as having ADHD, according to the 1998 National Survey of Mental Health and Wellbeing, Child and Adolescent Component.⁹ Professor Schweitzer noted that while more boys than girls are diagnosed with ADHD in childhood, diagnoses are relatively balanced by gender in adulthood.

Experts suggest that 15% of children with ADHD continue to experience full syndrome persistence (as assessed by DSM-IV-TR criteria) at 25 years of age and that as many as 40–60% of children with ADHD do not fully outgrow it; they continue to struggle with symptoms in adulthood, with some symptoms associated with clinical and psychosocial impairments persisting.¹⁰ That 15% of children with ADHD continue to experience full syndrome persistence into adulthood is controversial: the question of how applicable the DSM-IV-TR criteria are to adults is under active debate. Notably, the DSM-V draft criteria, available on the American Psychiatric Association website, have apparently made an attempt to broaden the criteria to include the adult population. Professor Schweitzer noted that ADHD probably wanes in adults from their 20s onwards.

The estimated prevalence of ADHD in the US adult population (aged 18–44 years) was 4.4%, according to data from the National Comorbidity Survey Replication (2001–2003), yet only 11% of the respondents had received treatment for ADHD in the previous 12 months.⁷ Similar estimates of prevalence have been reported worldwide, indicating that ADHD in adulthood is underdiagnosed and undertreated.

According to an analysis using genetic structural equation modelling of phenotype data from over 12,000 adults (twins, siblings and parents) registered with the Netherlands Twin Register, the heritability of ADHD in adults is estimated to be around 30% in men and women.¹¹ The study researchers reported that all familial transmission is explained by genetic inheritance; they failed to find any support for the hypothesis that cultural transmission from parents to offspring is important.

Recent research indicates a strong genetic basis, with the 7-repeat (7R) allele of the human dopamine receptor D4 (DRD4) gene implicated in the pathogenesis of ADHD.¹² The increased prevalence of the 7R allele in ADHD probands is consistent with the common variant-common disorder hypothesis, which proposes that the high frequency of many complex genetic disorders is related to common DNA variants. This recent analysis determined, by DNA resequencing of 250 DRD4 alleles obtained from 132 ADHD probands, that most ADHD 7R alleles are of the conserved haplotype found in a previous 600 allele worldwide DNA sample. However, half of the 24 haplotypes uncovered in ADHD probands were novel (not one of the 56 haplotypes found in those prior population studies). Over 10% of the ADHD probands had these novel haplotypes, most of which were 7R allele derived. The probability that this high incidence of novel alleles occurred by chance was much less than 0.0001.

Neuroimaging studies, such as that by Volkow and colleagues, have used positron emission tomography (PET) scanning to examine the caudate nucleus in ADHD adults and healthy controls.¹³ Volkow and colleagues found that in adults with ADHD, depressed dopamine activity in caudate and preliminary evidence in limbic regions (the hippocampus and amygdala) was associated with inattention and enhanced reinforcing responses to intravenous methylphenidate. These findings suggest that dopamine dysfunction may be involved with symptoms of inattention but may also contribute to substance abuse comorbidity in ADHD.

Impact on health & QOL of ADHD in adults

Recent studies have focused on life outcomes for adults with ADHD. Two key long-term studies funded by the National Institute of Mental Health evaluated two ADHD adult populations:¹⁴

1. The University of Massachusetts Medical School study (UMass study) conducted from approximately 2003 to 2004, examined lifestyle outcomes among three cohorts of adult patients: 146 clinic-referred adults with ADHD, 97 adults seen at the same clinic who were not diagnosed with ADHD but had a diagnosis of other psychiatric disorders, primarily anxiety disorders, and also a third general community sample of 109 adults without ADHD. In all groups, ages ranged between 32 and 38 years.

2. The Medical College of Wisconsin Study in Milwaukee (Milwaukee study), ongoing since 1977 (with the most recent follow-up conducted from 1999 to 2003), is an observational longitudinal study that has compared secondary lifestyle outcomes of 158 children who had been diagnosed with ADHD and, as adults, either continued to meet diagnostic criteria for ADHD or no longer have ADHD at the mean age of 27 years, compared to a community control group of 81 children without ADHD who were followed concurrently.

In both studies, the overall health of those with ADHD was poorer than that of controls. Quality of life was greatly and negatively affected by ADHD symptoms; all of the following health indicators were higher in the ADHD groups: body mass index; tobacco use; alcohol abuse or dependence; drug abuse or dependence; cholesterol; sexually transmitted disease.

Making the diagnosis in adults

Many clinicians have serious concerns and fears regarding diagnosis and treatment of ADHD in adults. One issue is that the diagnostic criteria remain controversial in adults. The current diagnostic criteria for ADHD were developed for children, and modifications are necessary to address the progression of the disorder into adulthood.¹⁵ Concerns and fears also exist regarding treatment with stimulants, in relation to their abuse potential and, to a lesser extent, their cardiovascular effects.

ADHD is often evident from 3 years of age. Retrospective assessments of childhood behaviour tend to reveal that symptoms of ADHD were apparent from very early on, rendering it a lifelong disorder. The DSM-IV-TR requirement that age of onset be prior to 7 years of age has caused much controversy; when seeking diagnosis in adults, not only is it frequently difficult to corroborate childhood memories, but adult recall is typically poor. Interestingly, DSM-V has increased the age of onset to 12 years. Nevertheless, many authorities argue that for adults, age of onset should be raised to 16 years.

Symptoms of ADHD differ in adults from symptoms in children, principally because the adult has learnt to live with the symptoms – to adjust and adapt, despite the symptoms still having the capacity to be very troublesome for the adult with ADHD and those around him/her.

Adult variants of inattention include failing to listen to instructions, not completing paperwork, feeling overwhelmed by large projects, missing deadlines, disorganisation – especially in relation to time management, forgetting commitments, and being late for appointments.

Adult variants of hyperactivity include trying to cover up or compensating for hyperactivity, e.g. choosing more active jobs and hobbies, restless and fidgeting in meetings and impatience whilst in queues, talking too much, frequently interrupting, making inappropriate comments.

Adult variants of impulsivity include excessive use of alcohol and tobacco, substance experimentation or abuse, driving too fast and motor car accidents, temper outbursts, sudden and many job changes, interrupting others, impulsive spending, and extramarital affairs.

DSM-V draft diagnostic criteria for ADHD

The DSM-V workshop on ADHD has issued consensus proposals for changes to the diagnostic criteria for ADHD as specified in DSM-IV available on www.dsm5.org. These proposals include: adding new criteria covering impulsivity; reducing the number of criteria necessary to diagnose ADHD in adults; and removing autism-spectrum and pervasive developmental disorders as exclusions for ADHD.

A useful mnemonic for recognising ADHD in adults is **S.C.R.I.P.T.** Clinicians should be alert to the possibility of ADHD in adults who exhibit problems with:

- **Self-Control**
- **Responsibilities and Restlessness**
- **Impulse-control**
- **Persistence towards tasks and goals**
- **Time management and organisation**

Screening instruments/tools

Screening scales and interviews provide an objective set of questions to structure the memory recall process about childhood symptoms and difficulties, reveal critical information about the severity and frequency of symptoms, and the impact of symptoms on functioning. They are only one component of a comprehensive evaluation; they may be used to supplement the diagnostic evaluation but are not sufficient alone for a reliable diagnosis of ADHD, advises Professor Schweitzer. Some of the self-administered and investigator-administered rating scales used in the assessment and diagnosis of adult ADHD are as follows:

Self-report scales:

- The WHO Adult ADHD Self-Report Scale (ASRS) – This self-report screening scale of adult ADHD was developed in conjunction with revision of the WHO Composite International Diagnostic Interview. The ASRS includes 18 questions about frequency of recent DSM-IV Criterion A symptoms of adult ADHD. The ASRS screener consists of 6 out of these 18 questions that were selected based on stepwise logistic regression to optimise concordance with the clinical classification.
- Barkley's Adult ADHD Quick Screen – This self-report screening tool is used to identify adults who may need further evaluation for ADHD. The scale consists of 13 questions, scored on a scale from Never (0) to Very Often (3). A cutoff score of 9 (out of 27 possible) suggests a very high likelihood that a person has ADHD.
- Brown Attention-Deficit Disorder Scale for Adults – This 40-item self-report measure is a quick way to screen for adult ADD. The instrument highlights 6 target areas: the ability to: sustain attention, sustain effort for completing tasks, activate and organise work tasks, recall learned material, utilise short-term memory, and regulate moods.
- Connors' Adult ADHD Rating Scales (CARRS) – These scales can be used to assess inattention, hyperactive-impulsive behaviors, and overall ADHD symptoms in adults over 18 years of age. CAARS include forms for self-reports and observer ratings that allow for information gathering from more than one source. Obtaining information from different people can improve accuracy of the results. Both versions contain 66 items, including 9 subscales. The scale also includes a measure to determine those respondents who might benefit from a more detailed assessment.

Observer-rated:

- Barkley's Adult ADHD Interview – This interview reviews history, domains of impairment, and other relevant areas of ADHD diagnostic criteria, as well as the most common comorbid disorders likely to be present with ADHD.
- Barkley's Quick Check for Adult ADHD Diagnosis – This 18-question interview identifies current and childhood ADHD symptoms, as well as areas of impairment.

Professor Schweitzer suggests that the Barkley's screening tools are very helpful for assisting clinicians who want to make a diagnosis or who feel unskilled in evaluating for ADHD.

Differential diagnosis of ADHD

A thorough history is essential in the differential diagnosis of ADHD, to exclude other psychiatric disorders. Symptoms of inattentiveness, hyperactivity and impulsiveness may be reported in a range of other psychiatric disorders, but none have the relatively *early onset* of chronic and impairing impulsiveness, distractibility; lack of persistence; executive and self-regulatory deficits of ADHD. Professor Schweitzer cautions that while the presence of the symptoms may alert clinicians to ADHD, they need to explore them more comprehensively. A key criterion of ADHD is that the disorder is *ongoing* – it does not wax and wane over time.

The extent to which diagnostic criteria in ADHD overlap with those in other conditions is depicted in Table 1.

Table 1. Overlapping diagnostic criteria in ADHD

	ADHD	GAD	Mania	Depression
Restlessness	X	X	X	X
Poor concentration	X	X	X	X
Increased motor activity	X	X	X	
Distractibility	X		X	
Irritability	X	X	X	X

GAD = generalised anxiety disorder.

Depression and ADHD

Adults with ADHD often have low self-esteem (having experienced failure at school, job, and in their relationships) and are demoralised, rather than being genuinely biologically depressed. Anhedonia, guilt, suicidality, appetite disturbance, poor sleep, are all indicators that are more likely to support a diagnosis of major depression. Mood disorders are typically (but not always) episodic. In contrast, the functioning of patients with ADHD is significantly impaired (poor attention, wandering mind, poor productivity) *all the time*.

Depression, Anxiety and ADHD

The chronic nature of dysthymic disorder can be more difficult to differentiate from ADHD in adults than are the features of major depression. Anxiety symptoms, panic attacks, excessive worrying, are not a feature of typical ADHD.

It is important that patients are reassessed after receiving treatment for anxiety or depression. Then is the time to review and treat ADHD symptoms. Professor Schweitzer emphasised that it is not necessary to rush to treat ADHD – the disorder has been there since childhood onwards (i.e. present for a long time).

Bipolar Disorder and ADHD

Bipolar II is more difficult to differentiate from ADHD than Bipolar I. A diagnosis of bipolar disorder is more likely if the patient history includes the following features:

- Cyclical, episodic disorder (a very important feature)
- Experiences sustained episodes of euphoria, increased energy
- Lack of need of sleep
- Family history of mood disorder
- Disorder started late adolescence (it is very unusual for bipolar disorder to occur any earlier).

Substance Abuse Disorder and ADHD

Clinicians should clarify whether the symptoms of inattention were present before the substance abuse commenced. It is very important to obtain collateral history reports from family interviews, school or work records, and suchlike.

Do the symptoms of inattention disappear during periods of sobriety? It is also important to note that some individuals self-medicate their ADHD with psychostimulants.

Clinicians should reassess for comorbidity of ADHD, after the substance abuse disorder has been treated and is in remission.

Personality Disorder (Borderline) and ADHD

While impulsivity, irritability, failed relationships and substance abuse are common to both disorders, it is much more the case that patients who are Borderline fear abandonment and that their relationships are volatile and marked by high emotional lability. In addition, suicide attempts and self-harm behaviour is much more likely in Borderline patients than in those with ADHD.

Thus, comorbid disorders are common in ADHD and can make accurate diagnosis difficult. Prevalence rates of ADHD comorbidity with other disorders are as follows:

- Major Depression/Dysthymia 27–32%
- Substance Abuse Disorders 20–30%
- Bipolar Disorder (adult onset) 10–20%
- Generalised Anxiety Disorder 11–45%

Diagnosing ADHD in adulthood

Clinicians should obtain a collateral history for all patients, advises Professor Schweitzer. Information is needed from partners, parents, siblings, etc., to confirm what patients report. School reports and employment history can provide evidence as to whether the patient performed poorly in school or has had low scores on evaluations at work. The evidence should demonstrate that the symptoms are not due solely to lack of effort, a poor vocational match, a transient situation, or an environmental circumstance.

Prioritisation of treatment:

- **First**, address and manage substance and alcohol abuse
- **Second**, treat disorders of mood
- **Third**, alleviate anxiety disorder
- **Fourth**, treat the ADHD when it continues to cause significant impairment in psychosocial functioning.

Professor Schweitzer advises that clinicians take time to make a definitive diagnosis; ADHD is not an emergency situation. Therefore, clinicians should first treat any substance abuse disorder, depression, anxiety – then reassess for ADHD – if still present and causing significant impairment, it does warrant treatment.

Stimulants

Stimulants remain the US FDA-approved medical treatment of choice for patients with ADHD and are associated with an exceptional response rate.¹⁶

- Methylphenidate (short- and long-acting forms): potently blocks reuptake of dopamine and modestly blocks reuptake of norepinephrine
- Dexamphetamine (short- and long-acting forms): potent blocker of dopamine and norepinephrine reuptake and promotes release of dopamine and norepinephrine from presynaptic neurons.

Notably, the short-acting formulations need multiple daily dosing. The long-acting forms are therefore better for dosing and are associated with less abuse potential. Clinicians need to be aware of the fact that methylphenidate has less addictive potential than dexamphetamine.

Nonstimulant medications

Nonstimulant medications are often considered when stimulants have failed or have caused intolerable side effects.¹⁷ Available options include atomoxetine (a selective

norepinephrine reuptake inhibitor), antidepressants (e.g. bupropion, desimipramine, tranylcypamine), modafinil, and clonidine.¹⁸

Atomoxetine is the only nonstimulant approved by the US FDA for the treatment of patients with ADHD. This treatment is effective and generally well tolerated in patients with ADHD. No studies provide direct comparative response rates for these therapeutic options, although one meta-analysis comparing stimulants and nonstimulants demonstrated a large overlap in efficacy among placebo-controlled trials.¹⁹ This analysis suggested that nonstimulants as a group may be less effective than stimulants for reducing core ADHD symptoms. Atomoxetine can be administered either as a single daily dose or split into two evenly divided doses, and has a negligible risk of abuse or misuse. This medication is therefore particularly useful for patients at risk of substance abuse, as well as those who have comorbid anxiety or tics, or who do not wish to take a controlled substance.^{16,20}

Some clinical evidence suggests that bupropion is helpful in ADHD, as are both desimipramine and tranylcypamine.^{16,21} Modafinil and clonidine have also proven helpful.¹⁶

Psychosocial treatment of ADHD

Over the last decade, evidence has shown that psychological treatment is helpful for the management of ADHD. Such approaches include:

- Psycho-education
- Cognitive Behaviour Therapy
- Support Person
- Couples Therapy
- Group Therapy.

Cognitive behaviour therapy can be very useful for helping individuals to manage ADHD:

- Time management and organisational skills
- Control of negative emotions and ideations
- Cognitive techniques to help with impulse control
- Cognitive restructuring, in relation to negative thoughts and self-talk
- Reframing of the past in context of a current diagnosis of ADHD.

Take-home messages – Professor Schweitzer

- ADHD is a disorder that begins in early childhood and commonly persists into adulthood, but goes largely undiagnosed and untreated.
- Controversy continues to surround the diagnosis and treatment of ADHD in adults.
- Effective treatment usually requires a biopsychosocial approach and nowadays, several effective treatments are available.

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Please consult all medication Data Sheets at www.medsafe.govt.nz before prescribing. Treatment decisions based on these data are the full responsibility of the prescribing physician.