

ADULT ADHD AND PSYCHOSIS:  
A REVIEW OF THE LITERATURE AND TWO CASES

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Abstract

Attention-deficit-hyperactivity disorder is a relatively common childhood condition, affecting approximately 3-4% of children. Recent studies have shown that the prevalence of this condition in adults is about 2.5%. ADHD is a well known co-morbid problem associated with many psychiatric disorders. Relatively little is known about the treatment of psychotic symptoms that arise in association with ADHD. In this article, the authors have described two cases presenting with psychotic symptoms along with a diagnosis of adult ADHD and have reviewed the available literature. The authors have suggested that although the combination of psycho-stimulants and antipsychotics is pharmacologically contradictory, it has been found to be safe and effective in the two cases described.

**Key Words:** Attention-deficit-hyperactivity disorder (ADHD), psychiatric conditions, psychostimulants, antipsychotics

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**Declaration of interest:** None

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Introduction

Attention-deficit-hyperactivity disorder (ADHD) is a chronic condition characterised by persistent and non-episodic symptoms of inattention, hyperactivity and impulsive behaviour (Asherson P et al. 2007). ADHD is a relatively common childhood condition, estimated to affect 3-4% of children (Asherson 2005). The UK National Institute of Health and Clinical Excellence (NICE) guidelines on ADHD have reaffirmed similar figures of 3-9% of school age children and young people in the UK and about 2% of adults worldwide. A meta-analysis of international studies (Simon et al. 2009) estimated the prevalence of ADHD in adults to be 2.5%, but added that this estimate is probably conservative because of the use of strict DSM-IV criteria for childhood ADHD that were applied in these studies. Those criteria are likely to underestimate adult ADHD. Furthermore, adult patients are also likely to be undertreated, as their treatment is commonly stopped before a significant reduction of symptoms occurs (McCarthy et al. 2009). This early discontinuation was explained by multiple factors such as older adolescents having greater autonomy over the decision making about their healthcare, young adults getting into employments which does not have the same demands for maintaining attention, but also the general lack of services for prescribing psycho-stimulant medication to adults. ADHD is regularly associated with other

psychiatric and neurological problems such as mood disorders, anxiety disorders, substance use disorders, impulse control disorders and tic disorders (Kessler et al. 2006, Kurlan et al. 2002). 20-25% of adult outpatients with depression, anxiety or substance abuse are estimated to suffer from Adult ADHD (Wilens et al. 2004). Rösler et al. (2004) found high prevalence rates of ADHD in prisoners, 45% in young males and a lifetime prevalence of 24% in female (Rösler et al. 2009) supporting the studies who have previously found poor social outcome in patients with ADHD (Simon et al. 2009).

There appears to be a paucity of literature regarding adult ADHD, co-morbid psychotic symptoms and the psycho pharmacological interventions recommended in this complex situation. Bellak et al. had suggested a separate diagnostic category of ADD Psychosis and differentiated it from schizophrenia on the basis of the different nature of co-morbid psychotic symptoms in ADHD as compared to schizophrenia. In this paper, we have reviewed the literature on this subject. We describe two case examples to suggest that co-morbid psychotic symptoms in ADHD can be treated with a combination of psycho-stimulants and antipsychotics. Both cases show transient psychotic symptoms in the context of borderline personality disorder and substance misuse, schizophrenia was excluded.

We have altered non-essential details in the case examples to preserve patient anonymity.

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## Case 1

Mr A is an 18 yr old male who was referred for psychiatric assessment by the general practitioner with problems of self harm, depression and delusional symptoms. In the 6 months prior to his referral his mood was reported to be low with loss of appetite. He was reported to be using cannabis regularly for at least 18 months but had already stopped smoking cannabis around the time of referral to secondary services. There was a breakdown of family relations. During his psychiatric assessment, three different problem clusters were identified in the form of psychotic symptoms, hyperactivity, and borderline personality disorder. He described hearing voices from the age of 13 which had been transient, but relatively persistent and continued to the time of referral. The voices were described as short-lived 2nd person auditory hallucinations. The patient experienced these voices as real. The content consisted primarily of derogatory comments about him or others. They commonly occurred in association with stressful events or significant substance misuse such as cannabis. These voices would lead him to verbally abuse and assault others. There was no convincing description of any Schneiderian first rank symptoms such as delusional perception, 3rd person auditory hallucinations in form of a running commentary or discussing the patient amongst themselves, thought alienation (withdrawal, insertion or broadcasting), thought echo or passivity phenomena. He described a history of hyperactivity going back to his early childhood. His mother always thought that he was hyperactive. He described himself to be chaotic as a child. He was always into everything which meant that he seemed to be active all the time. He had problems sleeping and used to have very little need for sleep which was not associated with elation. His school career was complicated by dyslexia. He did not achieve academically and was always disruptive in class. He was expelled from one school and was suspended many times. He described acting very impulsively when he was upset or feeling irritated by someone else. He has assaulted people with little provocation. He engaged in risk-taking dangerous activities impulsively including jumping off bridges. He thought that his hyperactivity was his most troublesome symptom. There was no obvious evidence of tics. He denied significant problems with inattentiveness. He scored 5/6 in part A and 8/12 in part B of the Adult ADHD Self-Report Scale (ASRS-v.1.1) indicating a very high probability of Adult ADHD. He did not fulfil DSM-IV criteria for schizophrenia or major depressive disorder.

His biological father abandoned the family home. He remembered his parents arguing a lot when he was young. He did not report physical or sexual abuse. His mother would often say hurtful things to him. He did not have any significant medical history. He reported drinking alcohol occasionally and sometimes getting very intoxicated. He tried cannabis for over a year but then discontinued. There is no significant forensic history, except being caught shoplifting once. He was on no medication at the time of first psychiatric assessment.

There was evidence of Borderline Personality

disorder which included difficulties trusting others, fear of abandonment and doing things to pre-empt being abandoned. He described chronic feelings of emptiness. He has cut himself occasionally in order to get rid of his anger and also to avoid hurting others. He described feelings of remorse and disliking hurting people.

He received a diagnosis of ADHD and Borderline Personality Disorder according to the DSM-IV criteria. There was no evidence of a depressive illness. He was started on a combination of methylphenidate 18mg once daily and amisulpride 200mg nocte, which was increased at two-week intervals. His hyperactivity and sleep improved and his friends noticed improvement in behaviour. He did not report any increase in the frequency of hallucinations. He was arguing and fighting less with others. The dose was increased according to response. There were periods of non-compliance in which his symptoms worsened and he became more chaotic again. He is currently being treated with methylphenidate XL 54mg and amisulpride 800mg daily. Irritability, hyperactivity, impulsivity, concentration and attention span all improved over a period of eighteen months. The auditory hallucinations became less severe and significantly less frequent. He is starting an art course in college and is coping well. He has not reported any side effects with this combination of medication.

## Case 2

Mr B is a 23 yr old male who was referred by his general practitioner for psychiatric assessment. When first seen by a consultant liaison psychiatrist, he was diagnosed as suffering from "auditory hallucinosis" according to his notes. He was started on gradually increasing doses of quetiapine. Quetiapine was reported to be partially effective in suppressing his transient auditory hallucinations but he had a tendency to experience angry and violent outbursts which got worse with subsequent interpersonal difficulties. The medication was then changed to aripiprazole as he also reported moderate sedation on the quetiapine dose of 50mg nocte. The dose of aripiprazole was increased to 15mg per day. Subsequent psychiatric assessments in a secondary care setting described him as experiencing transient 2nd person auditory hallucinations lasting from a couple of minutes to a few hours since the age of 14 years. The patient described these voices as real. The content could be derogatory as well as comforting. The voices occasionally told him to hurt or kill himself but the patient was able to distract himself and resist at times. There was no other evidence of any Schneiderian first rank symptoms, mania, depression, tic disorder or OCD. There was no relevant medical history. He did not fulfil DSM-IV criteria for schizophrenia. He reported regular cannabis use.

His developmental milestones were reported to be normal. He was sexually and emotionally abused by his father. He first started self harming by cutting himself at the age of 13, usually following stress or arguments with his mother. His academic achievements at school were average. He was bullied at school. He had several relationships which did not seem to last for

more than nine months. He described difficulty trusting people, fear of abandonment but he was currently in a supportive relationship. He received a diagnosis of Borderline Personality disorder. He was started on amisulpride 200mg nocte and aripiprazole was tapered off and stopped. At follow-up he described significantly fewer problems with auditory hallucinations; in fact his voices were almost entirely controlled. His cannabis intake also reduced significantly. During a follow-up appointment with one of the authors (PL), he reported problems concentrating on tasks at hand and needing lists to enable him to use certain equipment in the house. He described his mind as wandering as well as problems with planning. He reported himself to be very clumsy and does not often think about the consequences of what he is doing. He described himself as being quite impulsive. As a child, he was described as being overactive. His mother used to beat him up for breaking things or being generally clumsy or having accidents. He always had trouble sleeping and would still be active in the night time as a child. He had problems with attention at school as the only thing that would hold his attention was art, drawing for hours, but he would end up drawing on tables, walls etc. He worked as a labourer on building sites and in factories but was currently unemployed. He scored 5/6 in part A and 6/12 in part B of the Adult ADHD Self-Report Scale (ASRS-v.1.1) indicating a very high probability of Adult ADHD. The diagnosis of Adult ADHD was considered after confirming the likelihood of Childhood ADHD in discussion with a Consultant Child and Adolescent Psychiatrist who did not know him in the past.

Although his auditory hallucinations diminished with amisulpride 400mg nocte, he was unchanged regarding his impulsivity, and still had problems concentrating and planning, with irritability and hyperactivity. He was therefore started on methylphenidate 18mg. His diagnosis continued to be Borderline Personality Disorder and Adult ADHD. He is currently being treated with a combination of amisulpride 400mg nocte and methylphenidate XL 36mg. At the last follow-up he continued to be much better clinically regarding auditory hallucinations, impulsivity, concentration, planning and irritability. He did not report any side effects.

## Literature review and discussion

Symptoms in both patients improved significantly on a combination of amisulpride which is a dopamine receptor blocker and methylphenidate (a sympathomimetic psycho-stimulant). As far as we are aware, there appears to be no literature suggesting the combined use of methylphenidate and an antipsychotic in adult ADHD and co-morbid psychotic symptoms. However, there is clear evidence of the psychogenic potential of psycho-stimulants (Berman et al. 2009); including stimulant-induced psychosis (Greiner 2008). But there was no worsening of psychotic symptoms in the two patients described above, despite having been on such a combination for a period of more than a year. There is no clear guidance available for the clinician in cases of combined psychotic symptoms and persistent ADHD because of the lack of evidence base knowledge

regarding this combination of psychopharmacological agents. The evidence available so far for this kind of clinical situation is limited to seven case reports giving conflicting information as to how to treat patients presenting with such a complex combination of symptoms.

Huey et al. (1978) reported a patient who was diagnosed as suffering from chronic paranoid schizophrenia. Neuroleptics were minimally effective. Because of the patient's childhood history of Minimal Brain Dysfunction, he was enrolled in a double blind, placebo-controlled study to assess the effects of intravenous methylphenidate on his psychiatric condition. After injection with methylphenidate, the patient stated that the hallucinations faded into "babbling" and "white noise". He was less anxious and was in better contact with the interviewer. After this, the patient was reported to be maintained on oral methylphenidate. The improvement was persistent and not transient. He was not on a combination of neuroleptics and psycho stimulants. In that case report, the authors speculate that some of the schizophrenics who show favourable responses to psycho-stimulants may be those having childhood histories of Minimal Brain Dysfunction or an adult variant of MBD.

Bellak et al. (1987) proposed that Attention Deficit Disorder (ADD) may have a fundamental impact on the development and eventual structure of the personality, in some cases affecting the ego functions and predisposing the individual to psychosis during the tumultuous years of late adolescence and early adulthood. Confusingly, they suggested a separate classification for ADD psychosis in the psychiatric nomenclature. They clearly described ADD psychosis to be different from schizophrenia. They describe ADD psychosis as having the following features: rare or no hallucinations (if present, simple and brief), delusions, which, if present, are not well systemized and transparently compensatory for a low self-esteem, intermittently poor reality testing due to poor object relations, poor impulse control, impaired judgement, concrete thinking with little disorganisation of thought, little or no social withdrawal, loss of impulse control which is clearly reactive and characteristic, soft neurological signs, increased mood lability, low frustration tolerance, temper outbursts, difficult delivery, hyperkinetic infancy, later learning difficulties, short attention span, dyslexia, dysgraphia, physical awkwardness and clumsiness, family history of dyslexia and other learning disabilities, lack of response to or worsening by neuroleptics and favourable response to amphetamine like drugs and tricyclic antidepressants. They suggested a good prognosis in the short term but the long term prognosis includes social pathology e.g. alcoholism, criminality, job loss, and self-discharge from hospital with recurrence of brief episodes. They illustrated this description with three cases. Case 1 was of a 20 year old woman who had been in 8 hospitals during the previous 2 years, always with a diagnosis of schizophrenia. Upon neuropsychological testing, it was found that this patient suffered primarily from Minimal Brain Dysfunction (MBD), with some indication of psychotic phenomenon of a schizophreniform nature. She had an early history of learning difficulties. There was evidence of periodic explosive behaviour. There

was a family history of learning difficulties. This woman had reacted unfavourably to phenothiazines, and her only hallucinatory and delusional experiences occurred while she was on chlorpromazine. At no time did she show classical thought disorder. This patient was then diagnosed with "attention deficit disorder with psychotic episodes". She was treated with a combination of methylphenidate hydrochloride (5mg three times a day), imipramine (75 mg nocte) and when this failed to control her tension and anger, lithium carbonate 300 three times daily was added, along with a retraining programme, and psychotherapy for her problems with low self esteem. It is not clear exactly what helped her get better and whether the diagnosis would withstand the scrutiny of today's criteria. Case 2 was a 40 year old woman, referred with a diagnosis of schizophrenia. Closer examination of her case yielded the impression of ADD psychosis because of the episodic nature of her poor reality testing and presence of soft neurological signs associated with the ADD syndrome. There was a family history of ADD, epilepsy, and suicide in a psychiatric institution. This patient responded favourably to 10mg imipramine, modified psychotherapy and advice to avoid overload in her lifestyle. There is no mention of detailed psychopathology in the description of this case. Case 3 was a man in his 20s, referred for consultation after several hospitalisations for what was considered to be schizophrenic episodes. His symptom picture included irritability, grandiose delusions and clang associations. He responded "very badly" to phenothiazines, with confusional states and panic. There was a family history of schizophrenia and manic-depressive illness. This patient was withdrawn from phenothiazines and reported to be recovered on a combination of methylphenidate and lithium carbonate. Bellak's conceptualisation of the existence of an ADD psychosis as a distinct entity has not been investigated further in psychiatric research.

Pine et al. (1993) described two adult patients with ADHD and co-morbid psychosis. They reported that one of their patients continued to receive a combination of molindone (antipsychotic) and dextroamphetamine for 18 months, before being tapered off the molindone after the resolution of her psychotic symptoms. Their second patient remained free from ADHD symptoms and delusions for about 3 years with a combination of fluphenazine and methylphenidate. Eventually, in both patients, antipsychotic medication was discontinued but psychostimulant continued to be prescribed. There is no mention of patients with florid psychotic symptoms, improving only with psychostimulants. Rather, they continued the psychostimulant as the sole treatment only after the resolution of psychosis.

Opler et al. (2001) suggested the sole use of psycho-stimulants in ADHD and co morbid psychosis. The basis of their suggestion were the case reports of Huey et al, Bellak et al. and Pine et al, as described above. Based on the proposal of ADD psychosis by Bellak et al, Opler stated that it becomes imperative to inform clinicians that patients presenting with both psychosis and ADD who respond poorly to neuroleptics may benefit from a therapeutic trial of psycho-stimulants. This is, according to Opler in contrast to patients with schizophrenia and other psychotic

disorders. They hypothesized that in adults with psychosis and ADD, psycho-stimulants ameliorate both attention deficits and psychotic symptoms by increasing perfusion to the frontal lobes.

Tossell et al. (2004) described an open label case series of five children, aged 8-15 years, with childhood-onset schizophrenia (COS) and co-morbid attention deficit hyperactivity disorder (ADHD). Four COS inpatients were given stimulants for co-morbid ADHD after stabilization of their psychosis with antipsychotic medication. A fifth COS inpatient received stimulants while still actively psychotic, despite concurrent antipsychotic treatment. They reported that the data obtained from a retrospective chart review indicated a significant improvement in ADHD symptoms with no significant worsening of psychosis. They suggest that ADHD co - morbid with childhood onset schizophrenia (COS) may be safely treated with a stimulant, once the psychosis is stabilised. They also emphasised the need for a systematic investigation of this question.

In an open label study, Kronenberger et al. (2007) described improvement of ADHD symptoms and aggression in 12-16 year old non-psychotic participants when quetiapine was used in combination with methylphenidate after a lack of response to methylphenidate alone. Biederman et al. (2008) reported that treatment with risperidone was associated with tangible but generally modest improvement of symptoms of ADHD in children with bipolar disorder. These studies do not appear to address the issue of adult ADHD and psychotic symptoms, although a combination of an antipsychotic and a psycho-stimulant has been used safely in these studies.

In summary, the literature on Adult ADHD and co-morbid psychotic symptoms is limited and conflicting in terms of phenomenology and treatment. The previous authors recommend the sole use of psycho-stimulants in such clinical situations, but paradoxically the patients had been treated with a combination of antipsychotics and psycho-stimulants in a few of these reports. Furthermore, the recommendations were made on the basis of only a handful of cases. In our cases, there was limited collateral information and neuro-psychological testing. The diagnosis of childhood ADHD was retrospective. However, they help to highlight the dilemma faced by the treating clinician in weighing up the risks and benefits of combining antipsychotics and psycho-stimulants in routine clinical settings. We found the combination of amisulpride with methylphenidate to be effective and safe in our patients. This may surprise as amisulpride reduces available dopamine whilst methylphenidate blocks dopamine transporter complexes, thus enhancing the availability of dopamine. However, they do both act on different parts of the pre-synaptic dopamine system. It may also be possible that the mere availability of dopamine in the synaptic cleft is not the primary mode of action for psycho-stimulant drugs, but rather their regulatory effect on post-synaptic cell-firing (Huber et al, 2007), which would help to explain why a reduction of available dopamine in the synaptic cleft does not lead to a worsening of ADHD symptoms. If that were the case the anti-psychotic effects of amisulpride would equally be maintained.

## Conclusions

The presentation of psychotic symptoms with Borderline Personality Disorder and ADHD poses a challenging question to the treating clinician. Although the combination of psycho-stimulants and anti-psychotics remains controversial, the presence of psychotic symptoms with ADHD should not put off the clinician from considering it. Randomised controlled trials are needed to evaluate this combination in a wider population and to formulate treatment guidelines.

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