

# Journal of Psychopharmacology

<http://jop.sagepub.com/>

---

## **Modafinil treatment of amphetamine abuse in adult ADHD**

N Mann and P Bitsios

*J Psychopharmacol* 2009 23: 468 originally published online 18 June 2008

DOI: 10.1177/0269881108091258

The online version of this article can be found at:

<http://jop.sagepub.com/content/23/4/468>

---

Published by:



<http://www.sagepublications.com>

On behalf of:



[British Association for Psychopharmacology](#)

**Additional services and information for *Journal of Psychopharmacology* can be found at:**

**Email Alerts:** <http://jop.sagepub.com/cgi/alerts>

**Subscriptions:** <http://jop.sagepub.com/subscriptions>

**Reprints:** <http://www.sagepub.com/journalsReprints.nav>

**Permissions:** <http://www.sagepub.com/journalsPermissions.nav>

**Citations:** <http://jop.sagepub.com/content/23/4/468.refs.html>

# Modafinil treatment of amphetamine abuse in adult ADHD

*Journal of Psychopharmacology*  
23(4) (2009) 468–471  
© 2009 British Association  
for Psychopharmacology  
ISSN 0269-8811  
SAGE Publications Ltd,  
Los Angeles, London,  
New Delhi and Singapore  
10.1177/0269881108091258

N Mann *Counties Assertive Outreach, The Point, Granite Way, Mountsorrel, Leicestershire, UK.*

P Bitsios *Counties Assertive Outreach, The Point, Granite Way, Mountsorrel, Leicestershire, UK;  
Department of Psychiatry and Behavioural Sciences, Medical School, University of Crete, Crete, Greece.*

## Abstract

Substance abuse is a frequent co-morbid condition of adult attention deficit hyperactivity disorder (ADHD). Treatment with conventional psychostimulants in adult ADHD with co-morbid stimulant abuse may be problematic. In this study, we report the case of a patient with adult ADHD with co-morbid amphetamine abuse who was treated successfully with the non-stimulant alertness-promoting drug modafinil. The drug resolved both the inattention/hyperactivity symptoms as well as the

amphetamine abuse. Modafinil may be a suitable candidate treatment for adults with ADHD and stimulant abuse.

## Key words

adult ADHD; amphetamine abuse; modafinil; psychostimulants; treatment

## Introduction

The prevalence of attention deficit hyperactivity disorder (ADHD) among school-age children is reported between 6% and 9% (Biederman, 1998) and the disorder persists into adulthood in some 60% of all patients (Elliott, 2002). The prevalence among adults is estimated at 4.5% (Wender, *et al.*, 2001). There is an over-representation of substance abuse disorders in adults with ADHD, with reported rates as high as 17–45% for alcohol dependence or abuse and between 9% and 30% for drug dependence or abuse (Wilens, 2004). Adults with ADHD and substance abuse have an elevated risk of other psychiatric disorders compared with individuals who have either diagnosis in isolation, and their substance abuse disorders are more severe compared with individuals without the ADHD diagnosis. Individuals with both diagnoses, typically have an earlier onset, a more protracted course, greater severity, more relapses and increased difficulty in remaining abstinent from the abused substance (Wilens, 2004).

The approved treatment for juvenile ADHD is the psychostimulant methylphenidate (MPH) and more recently the selective noradrenaline reuptake inhibitor atomoxetine. Treatment early in the course of ADHD has been shown to be associated with a reduced risk of later developing tobacco and other substance abuse (Wilens, *et al.*, 2003; Wilens, 2004; Upadhyaya, *et al.*, 2005). The adult ADHD is still a poorly defined condition and it is not yet clear which subtypes respond to which

treatment. There are reports on the efficacy of conventional psychostimulants such as amphetamines (Spencer, *et al.*, 2001), MPH (Faraone, *et al.*, 2004) and atomoxetine (Michelson, *et al.*, 2003) and one study showed that modafinil has potential for the treatment of adult ADHD (Taylor and Russo, 2000). In the United States, atomoxetine is the only approved treatment for adult ADHD, whereas in certain countries, there are no drugs currently approved for the treatment of adult ADHD. The problem is further compounded for adult ADHD with co-morbid stimulant abuse, where treatment with conventional psychostimulants is by definition contraindicated. In this study, we report our experience with a case of adult ADHD with co-morbid amphetamine abuse, wherein inattention, hyperactivity and amphetamine abuse have been greatly improved by administering modafinil, a non-stimulant alertness-promoting drug.

## Case report

A 30-year-old male Caucasian patient presented in the outpatient clinic. During his 12-year history of contact with psychiatric services, he had repeatedly presented with irritability, aggression with physical violence, frequent mood swings and drug (cannabis, amphetamine, procyclidine) and alcohol abuse. He had been treated unsuccessfully on an outpatient basis with oral and depot antipsychotics, mood stabilizers,

tricyclic antidepressants and selective serotonin reuptake inhibitors. A referral to the Drug and Alcohol Service had been equally unsuccessful. The patient had received over time the diagnoses of paranoid psychosis, schizoaffective disorder, drug-induced psychosis, depression, antisocial and borderline personality disorder. No organic causes or medical conditions had been identified that could fully account for his symptoms.

Developmental and past psychiatric and forensic history, corroborated by his parents, showed that he was a hyperactive, fidgeting and disruptive/temperamental child since his preschool years, long before his first contact with the forensic and psychiatric services. A detailed investigation of the nature of his past forensic contact and violence showed that this was associated more with impulsivity, difficulty in tolerating frustration and constant reward seeking behaviour, rather than calculated attacks associated with callous concern for the needs and feelings of others and lack of remorse. Importantly, his offensive behaviours predated the onset of any drug abuse. As a child, the patient was frequently in trouble with his peers and teachers because of his constantly hyperactive and reward-seeking behaviour. At the age of 11, he had become a shop-lifter, stealing sweets and toys and had already attracted police attention. At the age of 14, he was expelled from school, after assaulting a teacher and then started the abuse of street drugs. He soon developed a career in petty crime and frequent troubles with the law ensued, culminating in a custodial sentence for burglary. As a result, the patient did not acquire any real vocational skills or employment record. There was no financial independence or adult relationships. At the age of 30, he was still living with and supported by his parents, scoring only 65 on the Global Assessment of Functioning scale and 'very ill' on the Clinical Global Impression (CGI) Severity scale.

His drug and alcohol abuse was initially in the context of novelty and reward seeking behaviour with frequent binges on a constant background of random, rather than preferred substances. Eventually this shifted and he developed a preference for amphetamines. Indeed this had been clearly the case for the preceding five years, and interestingly, this coincided with cessation of criminal activity. He felt that the amphetamines eclipsed the effects of all other substances, which he gave up, to feed his need for the amphetamines alone. He stated that he needed to use them because they helped him to 'clear his mind' and 'to focus and feel calm'. Interestingly, he was faithfully spending a fixed amount of money per week to purchase the street amphetamine. This could not be accounted for by shortage of money, since his habit was supported by his parents who were prepared to meet any shortfall should he have felt it necessary. The regular and fixed pattern of spending on amphetamines was suggestive of 'self-medication'.

His current and most prevalent complaint was his constantly low dysphoric-irritable mood and his addiction to oral amphetamine. He stated that his main problem, as far as he could recall, was always his behaviour and his difficulty in controlling it. He saw the use of amphetamines as 'a necessary evil', which could only be tackled 'with the right medication'. He denied the presence or a history of hallucinatory or other

abnormal experiences. Delusional thinking was not evident, and the patient was insightful and pragmatic albeit with an obvious propensity for unwarranted irritability, stubbornness, short-temperness and aggression. Amphetamine-induced ticks were also evident. Inconsistent with a diagnosis of a personality disorder, he did not try to impress, negotiate, elicit sympathy or pity, threaten or relate with any otherwise manipulative manner. In sharp contrast to the intensity and severity of his presentation and history, the patient appeared insightful and pragmatic. On the basis of the corroborated history of symptoms consistent with ADHD in childhood, with hyperactivity and poor concentration persisting into adulthood and the presence of affective lability, stress intolerance, impulsivity and hot tempers, the patient was diagnosed as a case of adult ADHD according to the Utah criteria (Wender, 1995), complicated with amphetamine abuse. Previous diagnoses of paranoid schizophrenia and schizoaffective disorder were ruled out on the basis of mental state examination and the Mini International Neuropsychiatric Interview (M.I.N.I.) (Sheehan, *et al.*, 1998) because the patient could not tolerate lengthier structured diagnostic interviews.

Modafinil was introduced as monotherapy, initially at a dose of 200 mg in the morning. A distinct improvement in both his symptomatology and demeanor were evident within a week. He described himself as 'more relaxed and focused' and stated 'the temper outbursts were under control'. He was able to read, watch a movie and participate in a conversation without becoming 'restless' and irritable. He commented that the effect of the drug was somehow fading by mid-afternoon and he was asking for a second dose around the early afternoon hours. Modafinil was increased to 200 mg in the morning and the afternoon and a week later the patient was happy that this treatment made redundant his need for amphetamines. He appeared much improved in the CGI-Improvement scale. Six months following the introduction of modafinil, he described and was observed to be well and was not able to identify any symptoms or difficulties. At this point, he also felt that he was capable of pursuing an avenue of work. At one year, the status quo was indeed maintained and he was taking a dose of modafinil at 200 mg twice daily.

## Discussion

This case illustrates the challenges and difficulties surrounding the diagnosis and treatment of adult ADHD. Aggregate findings from open and controlled trials suggest that in adults with ADHD with a co-morbid substance abuse disorder, ADHD medications marginally treat the ADHD but have little effect upon substance abuse or cravings. In a large, prospective, double blind, randomized trial of methylphenidate in cocaine abusing subjects, with clinical evidence of ADHD (Schubiner, *et al.*, 2002), some reductions in ADHD symptoms were noted, but no reductions in cravings or subsequent reductions in abuse were reported. On the contrary, modafinil has recently been

reported to promote abstinence in cocaine-dependent subjects during an 8-week placebo-controlled trial (Dackis, *et al.*, 2005).

Adult ADHD, particularly when complicated by substance abuse, is still a poorly defined condition and it is not yet clear which subtypes respond to modafinil or conventional stimulant treatment. It is, therefore, interesting that our patient's ADHD symptoms, together with amphetamine abuse, responded swiftly and convincingly to the introduction of modafinil in a sustainable way over time. Perhaps, one factor that favours a positive prognosis to modafinil treatment in adult ADHD with co-morbid amphetamine abuse is the stabilization of the abuse. A fixed pattern of use suggesting self-medication to resolve symptomatology rather than craving-driven abuse may be a stronger indication than that of severity or duration of the illness.

Modafinil is not an amphetamine-like agent and does not produce euphoria (Warot, *et al.*, 1993; Jasinski, 2000). Indeed, it blunts cocaine-induced euphoria in control laboratory conditions (Malcolm, *et al.*, 2002; Dackis, *et al.*, 2003). Its profile upon cognitive functions is distinct from that of conventional stimulants such as MPH, leaving unaffected cognitive domains selectively responsive to dopamine, such as working memory (Turner, *et al.*, 2004). Although a well-defined mechanism of action has not yet been elucidated, one of the key differences between conventional stimulants and modafinil is their effects upon arousal. Conventional stimulants such as amphetamine and MPH exert their arousing effects through both catecholaminergic and histaminergic activation, whereas modafinil is postulated to act through selective activation of the histaminergic system (Stahl, 2002a,b; Swanson, 2003). Patients with ADHD may require careful dose titration (Swanson, 2003) and an understanding of the dose-response curve of modafinil is necessary for a full clinical effect to be observed. It is notable that our patient maximized the clinical effect of modafinil by self-titrating the dose to 200 mg in the morning and 200 mg in the afternoon, a time-point which coincides with a circadian nadir in arousal. This is interesting in the light of recent evidence that modafinil reverses this circadian effect upon arousal (Nicolaou, *et al.*, 2008).

### *Implications for clinical care*

Adult ADHD can be hard to recognize because multiple layers of problems and diagnoses may add up throughout the years. Careful and corroborated developmental history may be the only clue as this case reports, perhaps together with an insightful, lucid and pragmatic presentation, infrequently seen in patients with personality disorders. The diagnostic and therapeutic problems can be worse when this condition is complicated with substance abuse. Persistent preference for stimulants can be a clue, especially when the abuse has been stabilized and the pattern suggests self-medication to resolve symptomatology rather than craving-driven abuse. This case suggests that under such circumstances, it may be worth considering modafinil monotherapy, allowing for a self-titration scheme.

### References

- Biederman, J (1998) Attention-deficit/hyperactivity disorder: a lifespan perspective. *J Clin Psychiatry* 59: 4–16.
- Dackis, CA, Lynch, KG, Yu, E, Samaha, FF, Kampman, KM, Cornish, JW, Rowan, A, Poole, S, White, L, O'Brien, CP (2003) Modafinil and cocaine: a double-blind, placebo-controlled drug interaction study. *Drug Alcohol Depend* 70: 29–37.
- Dackis, CA, Kampman, KM, Lynch, KG, Pettinati, HM, O'Brien, CP (2005) A double-blind, placebo-controlled trial of modafinil for cocaine dependence. *Neuropsychopharmacology* 30: 205–211.
- Elliott, H (2002) Attention deficit hyperactivity disorder in adults: a guide for the primary care physician. *South Med J* 95: 736–742.
- Faraone, SV, Spencer, T, Aleardi, T, Pagano, C, Biederman, J (2004) Meta-analysis of the efficacy of methylphenidate for treating adult attention-deficit/hyperactivity disorder. *J Clin Psychopharmacol* 24: 24–29.
- Jasinski, DR (2000) An evaluation of the abuse potential of modafinil using methylphenidate as a reference. *J Psychopharmacol* 14: 53–60.
- Malcolm, R, Book, SW, Moak, D, DeVane, L, Czepowicz, V (2002) Clinical applications of modafinil in stimulant abusers: low abuse potential. *Am J Addict* 11: 247–249.
- Michelson, D, Adler, L, Spence, T, Reimherr, FW, West, SA, Allen, AJ, Kelsey, D, Wernicke, J, Dietrich, A, Milton, D (2003) Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies. *Biol Psychiatry* 53: 112–120.
- Nicolaou, A, Schiza, S, Giakoumaki, SG, Roussos, P, Sifakas, N, Bitsios, P (2008) The 5-min pupillary alertness test is sensitive to modafinil: a placebo controlled study in patients with sleep apnea. *Psychopharmacology* 196: 167–175.
- Schubiner, H, Saules, KK, Arfken, CL, Johanson, CE, Schuster, CR, Lockhart, N, Edwards, A, Donlin, J, Pihlgren, E (2002) Double-blind placebo-controlled trial of methylphenidate in the treatment of adult ADHD patients with comorbid cocaine dependence. *Exp Clin Psychopharmacol* 10: 286–294.
- Sheehan, DV, Lecrubier, Y, Sheehan, KH, Amorim, P, Janavs, J, Weiller, E, Herqueta, T, Baker, R, Dunbar, GC (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 59(Suppl. 20): 22–33.
- Spencer, T, Biederman, J, Wilens, T, Faraone, S, Prince, J, Gerard, K, Doyle, R, Parekh, A, Kagan, J, Bearman, SK (2001) Efficacy of a mixed amphetamine salts compound in adults with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 58: 775–782.
- Stahl, SM (2002a) Awakening to the psychopharmacology of sleep and arousal: novel neurotransmitters and wake-promoting drugs. *J Clin Psychiatry* 63: 467–468.
- Stahl, SM (2002b) Psychopharmacology of wakefulness: pathways and neurotransmitters. *J Clin Psychiatry* 63: 551–552.
- Swanson, JM (2003) Role of executive function in ADHD. *J Clin Psychiatry* 64: 35–39.
- Taylor, FB, Russo, J (2000) Efficacy of modafinil compared to dextroamphetamine for the treatment of attention deficit hyperactivity disorder in adults. *J Child Adolesc Psychopharmacol* 10: 311–320.
- Turner, DC, Clark, L, Dowson, J, Robbins, TW, Sahakian, BJ (2004) Modafinil improves cognition and response inhibition in adult attention-deficit/hyperactivity disorder. *Biol Psychiatry* 55: 1031–1040.
- Upadhyaya, HP, Rose, K, Wang, W, O'Rourke, K, Sullivan, B, Daegas, D, Brady, K (2005) Attention deficit hyperactivity disorder, medication treatment, and substance use patterns among

- adolescents and young adults. *J Child Adolesc Psychopharmacol* 15: 799–809.
- Warot, D, Corruble, E, Payan, C, Weil, J, Puech, A (1993) Subjective effects of modafinil, a new central adrenergic stimulant in healthy volunteers: a comparison with amphetamine, caffeine and placebo. *Eur Psychiatry* 8: 201–208.
- Wender, PH (1995) *Attention-deficit hyperactivity disorder in adults*. New York: Oxford University Press.
- Wender, PH, Wolf, LE, Wasserstein, J (2001) Adults with ADHD: an overview. *Ann N Y Acad Sci* 931: 1–16.
- Wilens, TE (2004) Attention-deficit/hyperactivity disorder and the substance use disorders: the nature of the relationship, subtypes at risk, and treatment issues. *Psychiatr Clin North Am* 27: 283–301.
- Wilens, TE, Faraone, SV, Biederman, J, Gunawardene, S (2003) Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics* 111: 179–185.