The Management of ADHD in Children and Young People

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Chapter 15

ADHD and substance misuse in young people

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Introduction

Substance misuse is one of the most common public health problems in adolescence. Many young people who engage in the misuse of drugs and alcohol have multiple antecedent and coexisting mental health problems, and substance misuse takes a high toll in terms of healthcare costs, violent crime, accidents, suicide, social and interpersonal difficulties, and educational impairment (Mirza et al. 2011). In Europe, the prevalence of alcohol misuse is high, with up to 90% of students aged 15 or 16 years having consumed alcohol and, on average, 21% of boys and 15% of girls having tried illicit drugs at least once. About 38% of young people report that they have engaged in 'heavy, episodic drinking' (binge drinking, defined as consuming five or more drinks per occasion) during the past 30 days (European School Survey Project on Alcohol and Other Drugs (ESPAD) 2015, reported in Hibell et al. 2009). According to the 2013 British Crime Survey (Home Office 2014), 16.3% of young people aged 16–24 years had taken an illicit drug in the last year, and the lifetime use of illicit drugs was 36.7%. Tobacco, alcohol and cannabis were the most commonly abused substances, with cocaine and heroin accounting for less than 10% (Home Office 2014; ESPAD 2015).

ADHD is a common, heterogeneous neuropsychiatric condition that can persist into adolescence (Taylor et al. 1996) and adulthood (Biederman et al. 2006). Over the past decade, a robust body of evidence has emerged to indicate that the overlap between substance misuse and ADHD is larger than expected by chance (Mirza et al. 2012).

Clinicians trying to help people who have both problems face many uncertainties. It is often unclear how an individual should be assessed and advised, and what forms of treatment should be offered. Specialist services for one condition sometimes exclude the other. National guidelines appear to be lacking. As ADHD is a risk factor for the development of substance misuse, clinicians would be helped by a secure knowledge of the developmental pathways involved in the transition from ADHD to substance misuse so that they could develop early-targeted interventions to prevent substance misuse.

This chapter aims to bring together information about the comorbidity of ADHD and substance misuse and to make clinical recommendations about managing the combination of problems. We shall use the term 'substance misuse' throughout this chapter to refer to problematic substance use, including harmful use and substance dependence as described by the International Classification of Disorders (WHO 1993). The term 'substance misuse' as used in the UK is roughly equivalent to substance use disorder as described in the 5th edition of the Diagnostic and Statistical Manual of Disorders (American Psychiatric Association 2013). However, adult classification systems are inadequate in capturing the developmental stages of substance use in young people and may potentially prevent earlier interventions in young people who are at risk of developing severe forms of substance misuse in late adolescence or adulthood (Gilvarry et al. 2012).

How common is substance misuse in ADHD and ADHD in substance misuse?

Prospective, longitudinal follow-up studies conducted in community samples and clinical populations show that children with ADHD are at high risk of developing substance misuse (Barkley et al. 2004; Biederman et al. 2006). A recent meta-analysis of 27 longitudinal studies that prospectively followed children with ADHD into adolescence and adulthood showed that children with ADHD have a 1.5-fold increase in risk of developing any substance misuse and nearly three times higher risk for nicotine dependence than those without ADHD (Lee et al. 2011). Another meta-analytic study of 13 follow-up studies (Charach et al. 2011) showed that childhood ADHD was associated with alcohol misuse by young adulthood and with nicotine misuse by middle adolescence. The risk, however, may be due to other influences besides ADHD itself, such as coexisting conduct disorder or social adversity.

Conversely, studies in adolescent and adult populations attending substance misuse clinics have shown that between 20% and 30% have concomitant ADHD (Levin et al. 1998; Schubiner et al. 2000). Patients with both ADHD and substance misuse become dependent on substances at a younger age, use more substances and are hospitalised more often than substance misusing patients without ADHD (Arias et al. 2008). Persistent ADHD affects the onset, course and prognosis of substance misuse in adolescents and adults (see Mirza & Buckstein 2010 for a review).

Why and how does the association arise?

Developmental pathways involved in the transition from ADHD to substance misuse

The relationship between ADHD and substance misuse is complex and unlikely to reflect a single pathway. The possible reasons for the strong associations between ADHD and substance misuse may be direct or could be artefactual (e.g. resulting from the close link between ADHD and conduct disorders). This has implications for clinical input (Box 15.1).

Box 15.1: Possible reasons for the strong associations between ADHD and substance misuse

Possible cause for association	Strength of evidence	Clinical implications
Prenatal exposure to nicotine and possibly alcohol increase risk of development of ADHD →	Strong evidence for the role of nicotine use, less so for alcohol use →	Primary prevention efforts aimed at reducing maternal smoking during pregnancy
ADHD leads to substance misuse through the development of conduct disorders →	Strong evidence, especially if social adversity coexists →	Prevention efforts should involve detection and management of conduct disorders by offering psychological treatments
ADHD increases the risk for substance misuse – especially for nicotine dependence →	Evidence is equivocal →	Regular monitoring and preventive efforts to reduce the risk of development of nicotine dependence
Potential for ADHD medications to cause misuse of themselves or other substances →	No evidence so far to suggest increased risk, but diversion and misuse is possible →	Active treatment of ADHD is indicated, even if substance misuse coexists. Take steps to prevent diversion and misuse of stimulants
The effects of shared common causes such as genetic/neurobiological influences or psychosocial variables such as social deprivation →	Evidence so far is equivocal at this stage →	Public policy and prevention should pay more attention to address the putative risk factors
Self-medication hypothesis →	Very little evidence →	Active treatment of ADHD should reduce the risk of further misuse

A detailed analysis of the existing literature about the causal pathways and mechanisms of association between ADHD and substance misuse is beyond the scope of this chapter, and interested readers may refer to reviews by Mirza and Taylor (forthcoming). We shall, however, try to address one of the major questions that exercise clinicians at the coalface reality of clinical practice: does prescription of stimulants for ADHD increase the risk of substance misuse?

Are we at risk of doing more harm than good?

Review of evidence

Pharmacotherapy is a central component of interventions in children with ADHD, and there is a robust body of evidence to attest to the efficacy and safety of stimulants, and other drugs, at least in the short term (NICE 2006). Over the previous two decades there has been a substantial increase in recognition of the disorder and a corresponding rise in the number of children and young people treated with stimulant medication. In the UK, the numbers rose from an estimated 0.5/1000 children diagnosed 30 years ago to more than 3/1000 receiving medication in the late 1990s (NICE 2008). Epidemiological data from the UK database revealed a trend of increasing prescribing prevalence of ADHD drug treatment over the period 2003–2008 overall and for all age groups (McCarthy et al. 2012). However the numbers treated are much lower than published estimates of the prevalence of ADHD. Concerns have been expressed from a number of quarters regarding the exponential rise in the prescription of medications to control behaviour (Timimi 2002) and in particular about the potential risk of substance misuse as a result of prescribing stimulants to treat ADHD (Robbins 2002).

We shall aim to address this controversy by exploring the evidence from animal, clinical and pharmacological studies, followed by the clinical implications.

Animal studies

A large number of studies in rats have shown that methylphenidate, when administered parenterally, is quite similar to cocaine and amphetamine in terms of its reinforcing properties. At this stage, the data from animal studies regarding sensitisation are conflicting at best, and it is difficult to extrapolate the findings to human beings, for a variety of reasons (see Kollins et al. 2001 for a comprehensive review of animal studies). There are no well-designed studies to address this issue in human beings, so it is difficult to reliably answer the question 'Does early exposure to stimulant medication lead to sensitisation to stimulants or other drugs in later life?'

Pharmacological studies

All drugs of abuse act by increasing dopamine in the mesolimbic and mesocortical dopamine pathways (Robbins & Everett 2002). Like cocaine, stimulants used for the

management of ADHD exert their pharmacological properties by blocking dopamine reuptake, thereby increasing synaptic dopamine. Some studies have shown that methylphenidate is even more potent than cocaine in binding to the dopamine transporter and producing long-lasting neuronal adaptation in the nucleus accumbens (Kollins et al. 2001). Studies with healthy human volunteers have shown that the subjective effects of intravenous methylphenidate are quite similar to those of cocaine and amphetamine (see Kollins et al. 2001 for a comprehensive review). However, seminal studies by Volkow and colleagues from the National Institute of Drug Abuse have shown that the route of administration and dosages of stimulants are the most important variables that determine abuse potential (Volkow & Swanson 2003). When methylphenidate is administered intravenously, it enters the brain like cocaine and peaks rapidly, producing subjective sensations of euphoria. However, when methylphenidate is taken orally, the rate of uptake into the striatum is much slower, and subjective sensations of euphoria are significantly reduced or absent. Similarly, regardless of the routes of administration, methylphenidate is cleared from the body more slowly than cocaine, which may diminish the reinforcing properties and protect against repeated self-administration and misuse (Volkow & Swanson 2003). Thus, methylphenidate, when taken orally in therapeutic doses and within a clinical context, appears to be associated with a much lower abuse potential than cocaine.

Clinical studies

Randomised controlled studies of stimulant therapy thus far have not been long enough to determine any effect on later substance misuse. However, longitudinal community studies and naturalistic studies (which use the methodology of observing a subject's unaltered behaviour in his/her normal environment, without intervention) have followed children diagnosed with ADHD into adolescence or adulthood. A meta-analysis of prospective and retrospective studies conducted up to 2003 reported that those who had been treated with stimulants were protected against the development of substance-related problems (odds ratio of 1.9) compared with those who had not been treated in this way (Wilens et al. 2003). It is hard to be certain about which components of treatment were responsible – whether it was a direct effect of stimulants or the associated aspects of therapy. Interestingly, another recent meta-analysis of 15 studies published between January 1980 and February 2012 based on 2565 participants found that treatment of ADHD with stimulants neither protected nor increased the risk of later substance misuse (Humphreys et al. 2013).

Lambert and colleagues have argued that childhood ADHD and stimulant treatment is related significantly to rates of tobacco use and dependence and cocaine dependence (Lambert 2002). More recently, however, four prospective longitudinal studies have concluded that early stimulant treatment for ADHD does not contribute to substance misuse later in life and that, in fact, methylphenidate may delay the onset of continuous nicotine use (Manuzza et al. 2008; Biederman et al. 2008; Huss et al. 2008; Wilens et al. 2011).

A large-scale, 14-month randomised trial of intensive behavioural therapy against carefully crafted medication has reported on the naturalistic outcome (i.e. measured without offering any systematic interventions during the follow-up period) after the end of randomisation (Molina et al. 2007). At the 36-month point, those who had initially been assigned to behaviour therapy showed a substantial reduction in substance use compared with treatment as usual; medication alone did not appear to affect substance use one way or the other. There is some evidence to suggest that early age at initiation of treatment with methylphenidate in children with ADHD may have beneficial long-term effects on later substance abuse (Manuzza et al. 2008). Similarly, an 8-year follow up of the above National Institute of Mental Health Collaborative Multimodal Treatment Study of Children with ADHD (MTA Study) reported that medication for ADHD did not 'protect from, or contribute to, visible risk of substance use or substance misuse by adolescence', whether analysed as randomised treatment assignment in childhood, as medication at follow-up, or as cumulative stimulant treatment (Molina et al. 2013). Rates of substance use at all time points, including the use of two or more substances and substance misuse, were each higher in the ADHD than in the non-ADHD samples, regardless of sex.

A recent study based on a large-scale nationwide psychiatric cohort of ADHD patients of all ages diagnosed and treated in Denmark (n=20 742) investigated the risk of various medications including stimulants in comparison to a control group of non-medicated patients with ADHD (Steinhausen & Bisgaard 2013). The rates of substance misuse were higher in the non-medicated group, and treatment with stimulants did not increase the risk of substance misuse.

Clinical implications

What clinicians will want to take from the above brief overview is that children and young people who have been diagnosed with ADHD with coexisting conduct disorder are at significant risk for developing substance misuse, and prevention of this developmental path should be included as a routine goal of management. At least a substantial amount of the risk is mediated by the conduct problems (and/or the social adversity leading to them), thus suggesting that reduction of conduct problems and social adversity could be helpful in reducing the risk. The effect of behavioural therapy (in the MTA study) supports the inclusion of psychological and social measures in the long-term treatment of ADHD.

Even those with ADHD without conduct disorder are at considerable risk for cigarette smoking and possibly for other types of substance misuse, not least because they may develop conduct disorder later, again supporting the need for multimodal treatment of ADHD.

As stimulant medication does not appear to increase the risk of substance misuse, its use is not contraindicated. However, the lack of evidence for a self-medication theory

of substance use, except perhaps for nicotine, does not support the idea that risk for misuse is in itself an indication for 'preventive' use of stimulant medication.

Diversion and misuse of stimulant medication

Stimulant medications are controlled drugs and have themselves the potential for misuse and diversion, either for subjective euphoric effects or for effects on performance. Methylphenidate can be misused intranasally by crushing the tablets and snorting the powder or intravenously by dissolving the powder in water for injection. People who take the drug to induce euphoria prefer intranasal and intravenous routes, and there have been a few case reports of intravenous abuse of methylphenidate in young adults (Parran & Jasinsky 1991). Extended-release preparations of stimulants are less easy to misuse in this way than immediate-release tablets. More commonly, oral stimulants are misused to enhance performance in sports or some kinds of cognitive tasks and examinations (Wilens et al. 2008). A national survey of 10 904 college students in the USA reported that 4.1% of students had used stimulants for non-medical purposes in the past year, and 54% of students with ADHD on medication had been approached to divert their medication (sell, trade or give away) in the past year (McCabe et al. 2005). Although systematic information regarding the extent of diversion and misuse across the UK is not available, a study conducted in Wirrall, Merseyside, indicated that diversion was common, and the lifetime prevalence of illicit methylphenidate use in young people (31%) was second only to cannabis (Woolfall 2006). Another survey from the same area showed that pharmaceutical preparations of stimulants such as methylphenidate and dexamphetamine were available on the illicit market for as little as 30 pence a tablet (Geraghty 2008).

In summary, prescribed stimulants may be misused through multiple routes, including oral, intravenous and intranasal. In view of the risk of misuse and diversion of stimulant medication, caution should be exercised in the choice of medication, taking into account any personal and family history of substance misuse.

Guidelines for assessment and practical management

Young people presenting with substance misuse and ADHD pose significant challenges for assessment and treatment.

How to recognise and address substance misuse in patients with ADHD?

Children and adolescents with ADHD should be comprehensively assessed for substance misuse, but unfortunately many clinicians working in Paediatrics and Child and Adolescent Mental Health Services do not currently routinely screen young people for

substance misuse (Mirza et al. 2007). Defining substance misuse in young people is not easy. International classificatory systems such as the International Classification of Diseases (ICD-10; WHO 1993) and DSM-5 lack a developmental perspective in psychopathology, and categories such as 'harmful use', 'dependence' and 'substance use disorder' do not seem to capture all stages of substance use in young people (Mirza 2002). Based on the seminal work by Joseph Nowinski (1990), Mirza and Mirza (2008) and Mirza et al. (2011) proposed a developmentally sensitive and dimensional model to classify the stages of substance use in young people, starting with non-use, moving through stages of experimental, social, at-risk (prodromal) and harmful use, to substance dependence (Table 15.1). The above model has the potential to ascertain stages of substance use across the dynamic continuum and help clinicians choose the most appropriate intervention to suit the stage of substance misuse. Naturalistic follow-up studies show that a substantial minority of children who do not meet full criteria for substance misuse are at 'high risk' of developing harmful use/dependence during late adolescence or adulthood (Kandel 2002). From a clinical perspective, it is important to intervene at an early stage, before they have developed entrenched patterns of substance misuse, and the above classification offers a pragmatic choice. Readers may refer to the UK Practice Standards for the assessment and treatment of young people with substance misuse (Gilvarry et al. 2012) for more information.

Young people should be seen separately for a confidential interview. The attitude of the clinician should be flexible, empathic and non-judgmental in order to engage the young person in the assessment process and to obtain a valid estimate of their stage of substance misuse. Clinical and research experience shows that young people are generally more reliable than might be assumed, in terms of the information they can provide regarding substance misuse (Mirza et al. 2011). Explore the young person's leisure-time activities and gently guide them to talk about the nature and extent of substance use, context and impact on various domains of their psychosocial functioning. Detailed exploration of comorbid psychiatric disorders, other risk-taking behaviour and their relationship to substance misuse will help in formulating a differential diagnosis and treatment plan. Specific questions should be asked to determine whether the young person has used another person's drugs, given or sold medication to others, or increased the dosage of a drug without conferring with the doctors. Substance misuse is almost always not the only problem for most young people, and so a comprehensive developmental, social and medical history is a part of any complete assessment. Particular attention should be paid to the young person's vulnerability, resilience, hopes and aspirations. Evaluating the young person's readiness for treatment or stage of change (Di Clemente et al. 2004) may help to determine the initial treatment goals or level of care.

It is important to take a detailed family history, ideally with the help of a genogram, to determine whether there is substance misuse in biological relatives or other family members. Detailed information relating to peer group, including membership or affiliation of the young person to delinquent peer groups, should also be explored.

Specific treatment of substance misuse

Treatment modalities used in substance misuse are largely psychosocial. Although abstinence should remain the explicit long-term goal of treatment, harm reduction may be an interim, implicit goal of treatment, in view of both the chronicity of substance misuse in some young people and the self-limiting nature of substance misuse in others. Comprehensive treatment packages usually consist of individual, group and family/systemic therapies (Williams & Chang 2000). Medication should only be used as an adjunct. However, medication may offer a window of opportunity for young people to engage in psychosocial treatment (Mirza 2002, Marshall & Mirza 2007). Family therapy approaches, such as Multi-Systemic Therapy, Functional Family Therapy and Multidimensional Family Therapy, have the best evidence base for efficacy across a number of domains (Corless et al. 2009), although individual approaches such as cognitive behavioural therapy, either alone or in combination with motivational enhancement, have been shown to be efficacious as well (Waldron & Kaminer 2004). It has been shown that a single session of motivational interviewing (MI) can reduce the use of cigarettes, alcohol and cannabis in young people aged 16–20 years (McCambridge & Strang 2004). Clinicians should try to create links with local Substance Misuse Teams and aim to develop pathways of care to deliver comprehensive treatment for young people with ADHD and substance misuse (Gilvarry et al. 2012).

How can ADHD in patients with substance misuse be recognised and addressed?

The characteristic symptoms of impulsiveness, over activity and inattention can be elicited as in any assessment for ADHD. However, it is important to bear in mind that the clinical picture in adolescents with ADHD, whether they are misusing drugs or not, will show pathoplastic effects of age, and particular attention should be paid to emotional dysregulation, disorganisation and other executive function deficits. Screening questionnaires, informant interviews around past and current functioning, and school information remain relevant. In addition, it is necessary to gain a detailed history of the use of prescribed and recreational drugs. Some drugs (such as cannabis) can bring about inattentiveness, high-dose stimulants can produce marked over-activity (especially of a rather stereotyped form), and cocaine can produce a volatile emotional state. Clinical assessment therefore needs to establish whether the ADHD-type features preceded substance misuse, whether they are trait-like rather than episodic, and whether they have the characteristically disorganised quality of ADHD. Information from people who know the patient well, and knew them in childhood, is crucial for a reliable diagnosis. Repeated assessments may have to be carried out to clarify the diagnosis of ADHD once the substance misuse is stabilised or reduced, through specific interventions for substance misuse.

How should ADHD be treated in the presence of substance misuse?

Integrated, multimodal treatment of both substance misuse and ADHD has been found to be useful in clinical practice (Riggs et al. 2011; Mirza & Buckstein 2010), and specific

Table 15.1 Stages of substance (alcohol and drugs) use and suggested interventions: a pragmatic classification (Mirza & Mirza 2008; Mirza et al. 2011; Gilvarry et al. 2012)

Stage	Motive	Setting	Frequency	Emotional impact	Behaviour	Impact on functioning	Suggested interventions (Gilvarry 2000)
Experimental stage	Curiosity and risk taking	Alone or with peer group	Rarely or very occasionally	Effect of drugs is usually very short term	No active drug-seeking behaviour	Relatively little; may rarely result in dangerous consequences	Universal prevention (drug education, formal or informal)
Social stage	Social acceptance/the need to fit in	Usually with peer group	Occasionally	Mind altering effects of drugs are clearly recognised	No active drug-seeking behaviour	Usually no significant problems, but some can go on to show features of the early at-risk stage	Universal prevention (drug education, formal or informal)
Early at-risk stage	Social acceptance/peer pressure	Facilitated by peer group	Frequent, but variable, depending on peer group	Mind altering effects of drugs are clearly recognised and sought	No active drug-seeking behaviour, but develops a regular pattern of drug/alcohol use	Associated with significant dangers including recurrent binge drinking or problems associated with intoxication	*Targeted intervention/ treatment by non-specialist services (e.g. GP, school health worker, young people's counselling services, healthcare staff working in Child and Adolescent Mental Health Services (CAMHS), Paediatrics, etc.)

Table 15.1 (Continued)

Later at-risk stage (substance use is not dominating mental state)	Cope with negative emotions or enhance pleasure	Alone or with a like-minded peer group	Frequent/ regular use	Uses drugs to alter mood or behaviour	Active drug-seeking behaviour is a key indicator of this stage	May be impairment in functioning in some areas (e.g. school and family)	Treatment by specialist services (e.g. CAMHS), for both mental health issues and progression of substance use to further serious stages
Stage of harmful use (similar to ICD-10)	Drug use is the primary means of recreation, coping with stress or both	Alone or with an altered (drug using) peer group	Regular use, despite negative consequences	Negative effects on emotions and ability to function	Active drug-seeking behaviour, despite negative consequences across many areas of life	Impairment in almost all areas of life and/or distress within families or close relationships	*Treatment by specialist services (e.g. specialist substance misuse treatment services for young people and specialist substance misuse professionals within CAMHS)
Stage of dependence (similar to ICD-10; only a rare minority of young people progress to this stage)	To deal with withdrawal symptoms, and stop craving	Alone or with like-minded peer group	Compulsive, regular or often daily use to manage withdrawal symptoms	Emotional impacts of drugs are very significant; withdrawal symptoms prominent	Active drug seeking behaviour, often loss of control over use, pre-occupation with drug use, craving, and behaviour may involve criminality	Physical and psychological complications, impairment in all areas of life	*Treatment by specialist services including Detoxification and for some residential rehabilitation

*For some the involvement of agencies and services, other than substance misuse services, may be required.

Source: Modified and reproduced with permission from Mirza & Mirza (2008).

treatment for ADHD and substance misuse should ideally be provided under the same roof. Psychological treatment involving behavioural approaches and parental involvement has a strong place in the treatment of most people with ADHD (NICE 2008) and should also be available to young people using substances. Objective rating scales should be used whenever possible, to document improvement in target symptoms and adaptive functioning.

The most common drugs misused by young people include tobacco, alcohol and cannabis, and only a small proportion of young people use cocaine, heroin or ecstasy. Although abstinence is ideal prior to initiating medication treatment for ADHD, achieving complete or sustained abstinence may not be a realistic expectation for many young people, especially if they suffer from a coexisting untreated psychiatric illness. In practice, once the substance misuse (in the case of misuse of alcohol, cannabis and tobacco) is stabilised through harm-reductions strategies, it is reasonable to commence medication and other treatments for ADHD.

Interactions between drugs we prescribe and they 'prescribe'

Unfortunately, there is very little empirical data to inform clinical practice regarding the interaction between stimulant medication and drugs of misuse. The presence of alcohol or cannabis consumption is not a contraindication to stimulant prescribing, although clinicians should warn young people about the increased risk of side effects if they take alcohol and stimulants together. Concomitant cannabis and stimulant use should be closely monitored in those with a family history or past history of psychosis.

Misuse of cocaine and other stimulants

Although there is little empirical evidence to guide practice in those misusing cocaine and amphetamines (including methamphetamine), the similarity of the mechanism of action of the two drugs (inhibition of the dopamine transporter), albeit with different time courses, suggests that there could be particular dangers in the combination. Hence, such substance misuse, especially if it is chaotic as is often the case with regular amphetamine or cocaine misuse, should be addressed before initiating ADHD medications.

Misuse of opiates

The small minority of young people who present with opiate dependence often live chaotic lifestyles and tend to use a number of drugs other than opiates. It would be prudent to address the issues related to opiate dependence and other psychosocial issues first, before commencing medications for the treatment of ADHD. Stimulants can be used in conjunction with methadone or buprenorphine maintenance programmes, ideally in the context of a comprehensive psychosocial treatment programme to address their multiple complex needs.

Novel psychoactive substances (the so-called 'legal highs')

There is little empirical data to guide clinical practice, when young people are using the new psychoactive substances (NPSs, historically called 'legal highs') such as mephadrone or synthetic cannabinoids (spice), which are easily available through head shops and

the Internet. There is little information on the pharmacology, toxicology and safety of NPSs for humans. They can differ markedly in terms of their ingredients, potency, formulation and harmful effects, so the potential health implications of these compounds are largely unknown. In October 2015, the UK Government issued a blanket ban on all new NPSs. A pragmatic approach in managing comorbid ADHD and NPS misuse may involve addressing the misuse of these drugs first using principles of motivational interviewing and harm minimisation strategies and encouraging the young people to abstain from the NPS while they are receiving ADHD medications, in view of the scientific unknowns about the interactions between the above drugs. For up-to-date information about NPSs, see www.rednetproject.eu.

Evidence base for treatment of young people with ADHD and substance misuse

Although several medications including bupropion have been evaluated in open-label studies in adolescents with ADHD and substance misuse, there are only four published controlled trials (Table 15.2). In summary, although there is too little empirical data to assert the efficacy of medication in adolescents with ADHD and coexisting substance misuse, medication, including stimulants, appears to be safe and does not worsen substance misuse in the short term.

Beyond evidence base: The art and science of creating practice-based evidence

As we have seen so far, there is at present very little empirical evidence to guide treatment for coexisting ADHD and substance misuse. Creativity and a systemic perspective are

Table 15.2 Controlled trials of medications in young people with ADHD and substance misuse

Authors	No. of participants	Medication	Duration of trial	Results	Comments
Riggs et al. (2004)	69	Pemoline	12 weeks	Pemoline superior to placebo	Rare but serious hepatotoxicity
Szobot et al. (2008)	16	Long-acting MPH (MPH-SODAS)	6 weeks	Methyl phenidate superior to placebo	Small sample size, single blind trial
Thurstone et al. (2010)	70	Atomoxetine	12 weeks	ATX group not superior to placebo	Both groups received manualised MI/CBT*
Riggs et al. (2011)	360 (multicentre trial)	OROS-methyl phenidate	12 weeks	OROS-MPH group not superior to placebo	Both groups received manualised MI/CBT*

*MI/CBT: combination of motivational interviewing and cognitive behaviour therapy (CBT) throughout the 12-week trial, which addressed substance misuse.

essential to provide a treatment programme tailored to address the multiple complex needs that many such young people have. Clinicians should work to engage the 'hard to reach' young people in treatment (Box 15.2).

In our experience, creative use of motivational interviewing-based strategies such as exploring 'what is good and not so good about the drugs you prescribe and 'we prescribe' have helped break the ice and develop a collaborative relationship with young people (Boxes 15.3 and 15.4). An individualistic and flexible approach to prescribing has also been found to be helpful. For example, we have prescribed long-acting methylphenidate to young people who, following a period of intensive individual psychological treatment, have cut down their cannabis use to one or two nights per week (i.e. Fridays and Saturdays). They therefore ended up taking 'our drug' (long-acting methylphenidate) on five weekdays in the morning, followed by their 'drug' (cannabis) over the weekend. The above strategy, notwithstanding the risks involved, helped many youngsters to get back into mainstream education and helped achieve abstinence from cannabis in the long term.

Choice of medications to treat ADHD with comorbid substance misuse

There is a robust body of evidence from laboratory, clinical and neuroimaging studies to suggest that long-acting or controlled-release formulations are less likely to be misused than short-acting agents (Collins 2007). The abuse potential of oral methylphenidate is strongly influenced by its pharmacokinetic properties. The lower risk for misuse of extended-release formulations of methylphenidate is also related to the fact that its active components cannot be readily extracted (Wilens et al. 2006). The active compound contained in the osmotic controlled-release oral delivery system (OROS)-methylphenidate preparation is very difficult to extract by crushing, and the other long-acting stimulant formulations comprise long-acting beads that are not conducive to misuse by snorting, sniffing or injecting. These findings are consistent with a report on a group of adolescents with ADHD and substance misuse who were unable to achieve a high when attempting to inhale a preparation made from OROS methylphenidate (Jaffe 2002). However, despite their usefulness in producing high treatment adherence, whether treatment with extended-release stimulants is actually associated with a lower rate of misuse and/or reduced prevalence of substance misuse is a question that will require longer-term research.

Box 15.2: Clinicians can facilitate engagement in hard-to-reach young people in several ways

- ✓ Making use of the art of listening to young people – make them hear how they think!
- ✓ Appreciating the power imbalances in the therapeutic relationship
- ✓ Discovering the young person's strengths and resources
- ✓ Enhancing their motivation for change
- ✓ Instilling hope and rekindling their ability to dream about an alternative future

Box 15.3: Tips to use in a single-session MI-based assessment of substance use

- ✓ Assessment of substance misuse in the young is not rocket science! Clinicians working in CAMHS and Paediatrics already have the specialist skills to do the assessment.
- ✓ A safe space to talk and an empathic and non-judgmental stance from the clinician are crucial in encouraging young people to give details of their use of drugs and alcohol. Young people are more truthful than they are given credit for!
- ✓ The clinician facilitates rapport by expressing a genuine interest in and non-judgmental reactions to the young person's viewpoints and using language both familiar and similar to that of the clients.
- ✓ Collaboration works better than coercion: empathic listening and accurate reflection are crucial to facilitating change. If young people feel that they are truly understood and accepted by the clinician, they will be increasingly open to viewing the clinician as a valid consultant to their personal change process.
- ✓ Start off the assessment by asking about what they do for fun, what they get up to over the weekend – in a normative way. Ask for details of all drugs used, quantities, with whom, where, etc., including any risks endured.
- ✓ Establish the pattern of drug use and ascertain where they are in the developmental pathway/classification.
- ✓ You may choose to use one of the many strategies from motivational interviews (MI) to enhance their motivation to stop the use of drugs or to reduce harm.
- ✓ **Good things and Less Good things** (Box 15.4) is a useful strategy to use – especially in the early stages. It is useful for building rapport, and for understanding the context of substance use.

Box 15.4: The 'Good things and Less Good things' strategy for use in MI based assessment

- ✓ Use with clients who seem unconcerned, or when you are unsure about what they feel about their substance use. Resistance is minimised because you start with the positive things about the person's substance use.
- ✓ You talk about 'less good things' rather than 'concerns'. This allows the client to identify problem areas without feeling that these are being labelled as 'problematic'.
- ✓ Start off by asking the key question: 'What are some of the good things about your use of .....? (cannabis/alcohol)'. These usually emerge quickly. Summarise them if necessary. It may be helpful to write them down on one side of an A4 piece of paper.
- ✓ Then elicit the less good things about substances one by one, with the aim of finding out why this client thinks these are 'less good things'. Open questions are useful here, for example, 'How does this affect you?' or 'What don't you like about it?'. Write them down on the other side of the A4 sheet, so that you have a record of both on the same page.
- ✓ Summarise the good things and the less good things in 'you' language, as succinctly as possible, and leave the person time to react.
- ✓ For example: *'So using alcohol helps you relax... you enjoy doing this with friends, and it helps you when you are really fed up. On the other hand, you say you sometimes feel controlled by the stuff and that on Monday mornings you find it difficult to do anything at work'.*
- ✓ After the reflection, hand over the record of good things and less good things to the young person and ask them to reflect on it at home and add to/amend to it.

Lis-dexamfetamine dimesylate (LDX) is a promising new 'prodrug' formulation that could potentially reduce the risk of misuse of dexamphetamine by intranasal or intravenous routes. In its intact form, LDX is pharmacologically inactive. When taken orally, LDX is converted in the red blood cells by rate-limited enzymatic hydrolysis to L-lysine, a naturally occurring essential amino acid, and D-amphetamine. It has been proposed that this rate-limited conversion process may contribute to the extended duration of the effect that is seen throughout the day and a reduced 'drug liking' (Jasinski & Krishnan 2009), suggesting lower abuse potential. There is limited biotransformation of LDX when administered via parenteral routes. Double-blind crossover studies in adults with a history of stimulant misuse have suggested that the relative abuse potential of LDX was less than that for D-amphetamine (Jasinski et al. 2006). Early clinical experience is encouraging, but LDX has not yet been studied specifically in clinical populations with ADHD and comorbid substance misuse.

Atomoxetine, a selective norepinephrine reuptake inhibitor, has been reported to have little abuse potential, as evidenced by animal studies and small-scale studies in human volunteers (Heil et al. 2002; Wee & Woolverton 2004; Lile et al. 2006). Clinical experience is encouraging, although no randomised controlled trials have been carried out as yet to specifically assess the efficacy of atomoxetine in adolescents with ADHD and substance misuse. Meta-analytic studies and recent head-to-head studies have shown that the effect size of atomoxetine is somewhat lower compared to stimulants in the treatment of children and adults with ADHD without substance misuse (Faraone et al. 2006; Dittman et al. 2013). However, this issue is still arguable, and it has been suggested that the effect size of atomoxetine may become closer to that of the stimulants if a longer period of time (e.g. 12 weeks) is allowed and the person treated can tolerate the wait. However, in clinical practice, especially in young people with ADHD and comorbid substance misuse, we find that it is often difficult to achieve compliance with a longer period to full efficacy.

Guanfacine prolonged release is a new long-acting selective alpha 2-adrenoreceptor agonist, which has been shown to be effective in the treatment of ADHD, either alone or in combination with stimulants (Hervas et al. 2014) It has little abuse potential, although again, as yet, no clinical trials have been undertaken to attest the efficacy of guanfacine specifically in young people with people with ADHD and substance misuse.

The choice of a medication is dependent on the personal and family history of substance misuse, in particular the potential risk of misuse and diversion. In young people with non-chaotic substance abuse/dependence, and in the absence of significant family history of substance misuse, long-acting preparations of stimulant medications may be the preferred option, in view of their superior efficacy. However, if there is personal

or family history of stimulant misuse and the substance misuse is chaotic, non-stimulants such as atomoxetine or guanfacine should be considered as the drugs of choice (Box 15.5).

Strategies to reduce diversion of stimulant medication

Patients at high risk of substance misuse or those with coexistent substance misuse should be monitored closely to ensure that optimal treatment efficacy is being achieved and that stimulants are not being misused or diverted (Box 15.6). It is crucial to inform young people and their parents about the potential for stimulants to be diverted for illicit use. Involving the family and/or other caregivers can substantially improve compliance with treatment, and reduce the likelihood of diversion of medication. Pointers such as drug-misusing relatives, being in a drug-misusing peer group, the combination of absence of effect with ongoing requests for prescriptions, and frequent mysterious 'loss' of prescriptions, should alert clinicians to the possibility of diversion and misuse of prescribed medication.

Box 15.5: Choice of medication to treat ADHD with coexisting substance misuse

Non-chaotic substance abuse/ dependence with alcohol, cannabis or tobacco and no personal or family history of stimulant misuse	→	Long-acting preparations of stimulant medications (e.g. Concerta XL, Medikinet XL or Equasym XL, or lisdexamphetamine)
Personal or family history of stimulant misuse and the substance misuse is chaotic; IV opiate use	→	Atomoxetine or guanfacine–prolonged release

Box 15.6: Recommended close monitoring of drug treatment to prevent diversion

Consider the following:

- ✓ More frequent visits (weekly or biweekly)
- ✓ Initial prescribing of smaller amounts of medication
- ✓ Parental supervision of medication
- ✓ Thorough record keeping of all prescription drugs
- ✓ The use of urine drug screens or other investigations to monitor illicit substance use
- ✓ Education of individuals with ADHD and their families regarding safe storage of the medication

Box 15.7: Key practitioner messages

- ✓ Children with ADHD are at higher risk of developing substance misuse in adolescence and adulthood, and the risk is higher if there are comorbid conduct disorders and/or social adversity.
- ✓ There is a significant risk of development of nicotine abuse and dependence in people with ADHD, irrespective of the presence or absence of comorbid conduct disorder.
- ✓ The existing literature suggests that treatment of ADHD with medication does not increase the risk of the development of substance misuse.
- ✓ Misuse of stimulants employed for the treatment of ADHD is not uncommon, and stimulant medications are sometimes diverted and misused, either for subjective effects or for effects on performance.
- ✓ Integrated, multimodal treatment packages incorporating specific psychosocial and pharmacological treatment for substance misuse and other comorbidities such as conduct disorder should be provided along with optimal treatment of ADHD.
- ✓ Careful selection of agents for the treatment of patients with ADHD has the potential to limit drug diversion and misuse, particularly in high-risk groups such as those with a comorbid substance misuse or conduct disorder. Extended-release stimulants, non-stimulants or pro-drugs may be less likely to be misused or diverted.

Summary

- Substance misuse in adolescence is a major public health problem with substantial levels of morbidity and mortality. ADHD is a significant risk factor for the development of substance misuse through a number of complex causal pathways.
- Treatment of ADHD with medication is unlikely to increase the long-term risk of substance misuse. The risk of developing substance misuse is partly mediated by conduct problems (or the social adversity leading to them), and, therefore, psychosocial interventions should be offered as an integral part of the long-term treatment of ADHD, especially when there is psychiatric comorbidity.
- Young people with ADHD should be given specific information regarding the risk for substance misuse, and in particular the risk of development of nicotine dependence.
- Given the consistent findings of diversion and misuse of stimulants (either illicit use or for enhancing performance), clinicians, youth offending officers, substance misuse workers, teachers and other professionals should be made aware of the scope and context of the problem (Box 15.7).
- Specific programmes aimed at the prevention of substance misuse in children with ADHD and monitoring of prescription drug misuse and diversion should be developed with all stakeholders.

- Individuals identified with ADHD and comorbid substance misuse should be evaluated thoroughly for other complex needs and should be offered specific, evidence-based interventions to address both ADHD and substance misuse. The hope is that identification and optimal treatment of ADHD in children and adolescents may result in lower rates of substance misuse and diversion of stimulants, but further research is needed to establish whether this is in fact the case.

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