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Review of treatment for cocaine dependence.

Penberthy J.K., Ait-Daoud N., Vaughan M. et al. Request reprint Current Drug Abuse Reviews: 2010, 3, p. 49–62. DOWNLOAD PDF for saving to your computer

This comprehensive review found strong evidence that some drugs can help treat cocaine dependence and that cognitive-behavioural therapy is a powerful tool to manage cravings and stresses, especially when allied with effective pharmacotherapies.

Abstract Its immediate and powerful rewarding effects make cocaine one of the most addictive of drugs. Dependent individuals often experience difficulty abstaining due to cognitive impairment from repeated cocaine use, strong use-related social and environmental cues, and severe life stress. Cocaine use also affects areas of the brain related to movement, learning, emotion, and memory, further complicating effective intervention. Development of treatments for cocaine dependence has also been complicated by the tendency for patients not to complete treatment programmes and their propensity for relapse. Despite these challenges, some medications and some psychosocial approaches such as cognitive behavioural therapy have shown promise. Though dealt with below largely as if they were independent treatments, pharmacotherapies and behavioural therapies have been shown to have several added strengths when used in combination. Researchers have for example found disulfiram or topiramate allied with cognitive-behavioural therapy particularly efficacious.

Psychosocial interventions

Cocaine's addictive potential depends partly on the environment within which it used and on learnt cues and behaviours. Psychosocial therapies developed or tailored to treat cocaine dependence address these challenges directly. They include: motivational approaches to help patients clarify their ambivalence about using; cognitive-behavioural strategies to help them avoid/prevent triggers to using cocaine or use itself, and to cope without the drug; cognitive strategies to enable patients to think differently about their cocaine use; contingency management and community reinforcement programmes which systematically reward the patient for non-use; and meditation/mindfulness techniques to

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raise awareness of and enable detachment from sensations, thoughts, and cravings which may lead to cocaine use. Selected details below.

Cognitive behavioural therapies focus on the learning processes thought to underlie addiction and teach users new skills to cope with high-risk situations without using drugs. Individualised in interaction with the patient, these approaches orient users to the programme and ask them to set goals and establish a cognitive baseline in terms of their degree of confidence and commitment – useful also for therapists seeking to match therapeutic tasks to the patient. Then patient and therapist examine past, present, and anticipated future habits and triggers associated with using cocaine and try to formulate effective coping strategies and emergency plans to prevent stress situations leading to cocaine use. The aim is to unlearn old, counterproductive responses and learn new ones. Interventions based on cognitive-behavioural approaches have been relatively widely investigated over the last two decades. Clinical evidence indicates that the therapy helps patients overcome dependence not just on cocaine but also methamphetamine, tobacco, and alcohol, though in respect of cocaine, it has not always been found more effective than alternative therapies. One of its advantages is that substance use reductions seem to last longer than after other approaches. However, cognitive-behavioural therapies take time, practice and patience to assimilate. People who find difficulty with abstract reasoning may not receive the full benefits – a particular problem for cocaine users who have suffered neuropsychological impairment.

Approaches like contingency management and community reinforcement involve rewarding patients for desired behaviours, usually abstaining from specific forms of substance use. Contingent rewards may for example be shopping vouchers, while community reinforcement typically relies on the approval of friends and family and the chance to enjoy fulfilling activities with them incompatible with substance use. Often these two variants of a reward-based approach are deployed in combination. Both alone and in combination they enjoy some research support. The main effectiveness question over material rewards is whether the commonly observed intrate abstinence while cognitive-behavioural therapy or community reinforcement help sustain it by teaching enduring skills, changing thought patterns, and altering how the user's social circle responds to them.

Motivational interviewing and derivatives such as motivational enhancement therapies adopt a directive but client-centred approach intended to enhance motivation to change long-standing drug use patterns. Typically the approach involves expressing empathy, eliciting the contradictions between the patient's current behaviour and their objectives in life, avoiding explicit confrontation, and promoting self-efficacy. Widely applied to substance use disorders, these approaches have registered medium-sized effects in reducing substance use. However, the relatively small body of research in relation to cocaine dependence precludes a definitive analysis of their effectiveness. Very limited evidence suggests that motivational enhancement may promote engagement in therapy and more positive attitudes about the change process when combined with interventions such as cognitive-behavioural therapy.

Thought to increase awareness of and detachment from sensations, thoughts, and cravings that may lead to substance use, psychosocial interventions incorporating **mindfulness** and/or meditation (including Acceptance and Commitment Therapy, Dialectical Behavior Therapy, Mindfulness-Based Stress Reduction and Transcendental Meditation) have been linked to reductions in substance use primarily among non-abusing, non-dependent caseloads. Well-controlled studies are rare, and evidence in respect of cocaine dependence in particular is lacking.

Pharmacotherapies

Some medications which have shown promise as treatments for cocaine dependence seem to curb cocaine use by affecting the neurotransmitter systems through which it exerts pleasurable effects or by acting as a substitute stimulant. However, most are still in their infancy with regard to testing their clinical utility and large, long-term, well controlled studies are lacking. Also all the drugs are delivered orally, making them less useful if the patient is vomiting, and they have side effects which limit their use. Some may themselves be abused. Selected details below.

Formulated as an anticonvulsant to treat epilepsy, topiramate has been **found superior** to placebo in treating alcoholism. In-treatment cocaine use reductions seen in a few studies require confirmation and extension by larger placebo-controlled randomised trials testing different doses. Topiramate may affect craving and substance use by attenuating the desired effects of taking drugs. One problem is that while effectiveness may increase with higher doses, so too do undesirable side effects.

By inhibiting an enzyme needed to metabolise alcohol, **disulfiram** leads to aversive physical reactions if the patient drinks. It also affects blood levels of cocaine and of certain neurotransmitters in the brain, actions thought to account for any impacts on cocaine use. Overall, there is **good evidence** indicating that disulfiram shows significant promise for treatment for cocaine dependence, including a randomised trial in which it was compared against a placebo and was particularly effective in combination with cognitive-behavioural therapy. Possible psychotic reactions at high doses may limit its use in certain patients.

Ondansetron is one of a class of drugs which restrain the release of the neurotransmitter dopamine. It attenuates the cocaine 'high' and (in one small study hampered by high drop-out) has been found to curb cocaine use by dependent patients. Baclofen is prescribed to reduce muscle spasticity and is also believed to affect the cocaine-induced release of dopamine. It has been found to relieve craving for cocaine, but in one well controlled trial it did no better than a placebo in reducing cocaine use among dependent patients, except among the heaviest users.

Modafinil is (like cocaine itself) a stimulant which it was hoped would not only relieve the symptoms of cocaine withdrawal, but also act as a relatively non-addictive 'substitution' treatment similar to methadone for heroin. It has been found to reduce cocaine use among dependent patients, though in one trial only those not also dependent on alcohol.

Other medications considered or tried as treatments for cocaine dependence, but as yet inadequately tested or found ineffective, include acamprosate, carbamazepine, gabapentin, vigabatrin, tiagabine, buproprion, and the substitute stimulant methylphenidate.

The authors' conclusions

Strong evidence from controlled clinical trials shows that that drugs which modulate neurotransmitter and/or neural pathways involved in cocaine's effects, or which act as a substitute for cocaine, can help in the treatment of cocaine dependence. Among the psychosocial therapies, cognitive-behavioural therapy is a powerful tool to manage cravings and stresses leading to use. Combined with effective pharmacotherapy, it has the best research record in terms of retention in treatment and avoiding relapse after abstinence has been achieved. However, no treatment has yet been shown to completely and effectively treat cocaine dependence; each exhibits weaknesses in longitudinal studies where long-term abstinence is the primary outcome of interest. Much more research is needed to identify how effective these therapies are and for what types of patients, and in particular how to tailor them to enhance their acceptability to patients, improve retention in treatment, and prevent subsequent relapse.

FINDINGS In 2005/06 about 32% of patients in drug treatment in England were there primarily to address problems involving cocaine (powder or crack); by 2008/09, the figure had risen to 41%. Reflecting general population trends, among 18–24-year-olds in treatment the proportion with primary cocaine powder problems more than doubled from

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6% to 14%. Among those starting treatment, the latest figure was 18%. This pattern makes it likely that cocaine will figure even more in future years. In the absence (despite decades of searching) of a recognised drug-based treatment, and with no specific psychosocial therapy, services have turned to acupuncture, yet studies show that too fails to help. Serial disappointment might lead some to conclude that when it comes to cocaine and crack, 'nothing works'. But as the featured review found and as reflected in analyses published by Findings, this is far from the case. Almost any bona fide counselling or therapeutic approach helps some people some of the time, often many much of the time. It doesn't have to be very sophisticated, though cognitive-behavioural therapies have the most extensive research record, and some severe cases may need continuing support and residential care (1 2). In the latest English national drug treatment study, crack seemed easier to give up than heroin. Controlling one's crack use, the most addictive form of cocaine, is not easy but neither is it uniquely difficult.

National guidance from Britain's National Institute for Health and Clinical Excellence (NICE) recommended against cognitive-behavioural therapy as a routine treatment for drug problems in general, suggesting its main role was in tackling accompanying depression and anxiety. However, the analyses on which this was based did not show that cognitive-behavioural therapy was *in*effective, just that it was not convincingly *more* effective than other well structured therapies. If this is the case, then the decision between such therapies can safely be taken on the grounds of what makes most sense to patient and therapist, the therapist's training, availability, and cost. In respect of cost and availability, cognitive-behavioural therapy may (more evidence is needed) prove to have two important advantages. The first is that effects may persist and even amplify without having to continue in therapy. The second is that it lends itself to manualisation to the point where it can be packaged as an interactive computer program and made available in services lacking trained therapists – potentially a crucial advantage for widespread implementation. In the UK implementation has been held back by the shortage of therapists, an obstacle currently being addressed by a government-funded training initiative.

Thanks for their comments on this entry in draft to Jennifer Penberthy of the University of Virginia Health System Center for Addiction Research and Education in the USA. Commentators bear no responsibility for the text including the interpretations and any remaining errors.

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