DRUG & ALCOHOL FINDINGS *Review analysis*

Antipsychotic medications for cocaine dependence.

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Search for antipsychotic drugs to treat cocaine dependence has reached a dead end pronounces authoritative review. Psychosocial therapies remain the mainstay of treatment.

SUMMARY Antipsychotics have been candidates for the treatment of addiction for their ability to block dopamine [a naturally occurring 'neurotransmitter' chemical which transmits signals between brain cells] receptors in the brain and to offset the increase in dopamine-mediated brain activity related to use of drugs such as cocaine. The so-called 'atypical' antipsychotics like risperidone and olanzapine extend their action to other brain systems involved in drug addiction, of which interest has centred on the system mediated by the neurotransmitter serotonin. Furthermore, cocaine use can lead to symptoms mimicking psychosis, such as hallucinations and paranoia, symptoms which antipsychotics may relieve.

Based on reports published up to July 2015, the featured review amalgamated findings from trials which had randomly allocated adult cocaine-dependent patients to an antipsychotic medication versus a placebo or some other treatment. The reviewers found 14 such trials, which generally benchmarked the impacts of antipsychotics against an inactive placebo. Drugs tested in the trials included risperidone, olanzapine, quetiapine, lamotrigine, reserpine, haloperidol and aripiprazole.

Main findings

Across eight studies with 397 participants, compared to a placebo there was moderate-quality evidence that antipsychotic drugs reduced drop-out from treatment.

There were no significant effects in respect of any of the other primary outcomes assessed by the review: number of participants using cocaine during treatment; continuous abstinence, marked by negative drug screens for two to three weeks; and the number of participants experiencing at least one side effect. However, the evidence was of poor quality and came from few studies. Also found was low-quality evidence from just four studies showing no difference in craving for cocaine.

Of the individual drugs, only quetiapine seemed to perform better than placebo in reducing cocaine use and craving, but these results came from just two studies totalling 80 participants.

Key points
From summary and commentary

A systematic review which amalgamated findings from randomised trials concluded that while antipsychotic drugs may reduce drop-out from treatment for cocaine dependence, there was no reliable evidence that they reduced cocaine use.

No medications of any kind have yet gathered sufficient evidence to become an accepted treatment for cocaine dependence, though some show promise.

The mainstays of treatment are psychosocial therapies, and patients generally stop using cocaine more readily than heroin-dependent patients stop using heroin.

The authors' conclusions

The argument for using antipsychotics to treat problem cocaine use is based largely on their use in treating psychiatric complications – not the same as treating the substance use disorder itself. Antipsychotics are not risk-free medications; their side effects are not trivial and may be long-lasting. This review did not find evidence that they reduced cocaine use. As things stand, there is no evidence supporting the use of antipsychotic medications in the treatment of cocaine dependence, although results come from only 14 trials, with small sample sizes and moderate-to-low quality of evidence. Given the absence of promising results for reduction of drug use and the relevance of side effects, no further research seems to be justified to explore the effectiveness of this class of drugs in cocaine users without psychiatric comorbidities or complications.

It should be borne in mind that of the 14 included studies, 13 were conducted in the USA, limiting the generalisability of the results; health effects of various substances of abuse seem to be strongly dependent on social context, and the location of the studies could affect treatment impact.

Most of the studies did not report useful results on important outcomes such as side effects, use of cocaine during the treatment, and craving. In studies which did report them, it was not possible to amalgamate the results due to differences in how they were measured and reported. For the outcomes which were reported, generally there was appreciable risk that drop-out and other factors might have biased the results.

FINDINGS COMMENTARY For heroin there are effective pharmacological treatments like methadone to more safely and legally meet the patient's need for opiate-type drugs, and naltrexone to block the effects of opiates and promote abstinence. For cocaine, decades of searching have failed to find a recognised drug-based treatment. Now the featured review conducted under rigorous Cochrane procedures has said that in respect of antipsychotic drugs, it is time to declare the search a fruitless dead end. In their report on cocaine published in 2015, the UK's Advisory Council on the Misuse of Drugs acknowledged that "Across the world ... there is a consensus, amongst scientists, that the existing evidence provides weak, if any, support to the use of pharmacological treatment for cocaine abuse and dependence." Relying largely on a review from the British Association for Psychopharmacology published in 2012, they were, however, not entirely ready to throw in the towel on pharmacological treatments, considering it worth pursuing the possible roles of anti-craving agents such as disulfiram, modafinil, topiramate, and baclofen, and of 'cocaine vaccines' which stimulate the body to produce antibodies to cocaine

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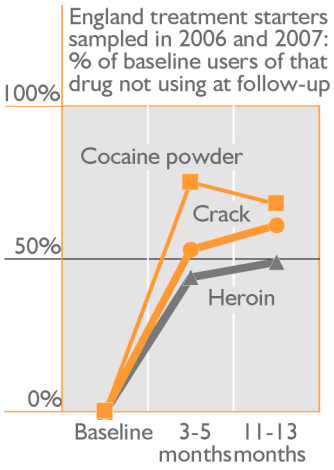
For the time being the Advisory Council on the Misuse of Drugs and the British Association for Psychopharmacology agree that (in the words of the latter's review) "Psychosocial interventions such as [cognitive-behavioural therapy] and contingency management remain the mainstay of treatment." As explored in an Effectiveness Bank hot topic, while there is no psychosocial therapy specific to cocaine or stimulant use, "just about any bona fide counselling or therapeutic approach helps some people some of the time, often many much of the time, and usually to roughly the same degree." The approach does not have to be very sophisticated, though severe cases may need continuing support and residential care (1 2).



Sometimes portrayed as uniquely addictive, neither cocaine powder nor smokable crack cocaine are particularly hard to stop using. In the latest English national drug treatment study, primary users of crack and cocaine powder were more likely to stop using than were primary heroin users. Of the heroin users who could be followed up (many patients were not), three to five months after starting treatment 44% had stopped using, and about a year after starting treatment, 49%. Corresponding figures for stopping crack use were higher at 53% and 61% respectively, and for cocaine powder, 75% and 68% ▸ chart.

The featured review's judgement that quetiapine is the antipsychotic with most evidence for cocaine use reductions highlights how weak the evidence is. Their verdict relied largely on a single US study. Of the 115 cocaine users who agreed to join the trial, just 60 started it and only 18 supplied final follow-up data 12 weeks later. The medication was a once-a-day long-acting formulation manufactured and supplied by Astra-Zeneca which sponsored the study and had given honoraria to the lead author. More than anything, the study showed that cocaine users were not attracted and retained by the treatment.

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REVIEW 2012 BAP updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP

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REVIEW 2009 Efficacy of opiate maintenance therapy and adjunctive interventions for opioid dependence with comorbid cocaine use disorders: a systematic review and meta-analysis of controlled clinical trials

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