Pharmacotherapy for Craving

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Summary

The term craving derives from common language and its use in scientific literature is still under discussion. Nevertheless it seems appropriate for describing the very essence of "addiction" as compulsion. The various clinical forms of craving have two main features: a potent reinforcing effect which is at the base of drug addiction and a negative reinforcement mechanism linked to phobic feelings aimed at avoiding withdrawal symptoms. Anticraving therapy should act on both of these aspects. After discussing the results obtained with the principal anticraving drugs, such as methadone, GHB, dopamine agonists (bromocriptine), desimipramine, mood stabilizers, and serotoninergic drugs, the results of personal studies in progress are discussed.

At present, knowledge about drug dependence seems to be characterized by a common denominator, craving. Craving could thus be defined a new psychopathological or syndromic entity which Marlatt argues, captures the essence of addiction, in terms of its compulsive qualities (1).

Wise identifies 2 types of craving on the basis of reinforcement. One type of craving is associated with positive reinforcement and is considered fundamental for the initiation of drug use, for the transition from use to abuse and may be responsible for relapse after a period of abstinence. The other type of craving is associated with a phobic mechanism, (which is a negative reinforcement) that aims at avoiding withdrawal symptoms, and is an important factor in maintaining dependence to opioids in particular (2,3).

The phenomena of craving has the following characteristics:
1. Strong desire for a substance or a situation.
2. Somatic symptoms related to the autonomic nervous system.
3. Drug or situation seeking behavior
4. Inability to stop drug or situation seeking behavior in spite of obstacles, physical danger or social consequences.
If craving is the base of addiction in the beginning of the natural history of drug use as well as in continued drug use (increasing doses and revolving door phase) its treatment may be essential to the "management" of drug dependence.

Observations that various substances have a common biological pathway of action related to craving opens the way to interesting hypotheses regarding polydrug abuse and the possibility of more reasonable therapeutic interventions. In fact, different substances stimulate the same neurotransmitter systems, triggering a positive reinforcement (4-12,2). The physical needs and craving experienced by the drug addict could be partially satisfied by other substances thus explaining polydrug abuse. The practice of polydrug abuse may arise not only because the substance of choice is not available but because craving has been inadequately treated.

The pharmacological agent suitable for the treatment of craving should alleviate withdrawal symptoms and interact with the positive reinforcement system. Most pharmacological agents used in the treatment of craving do not have these characteristics. For example clonidine is effective on withdrawal symptoms in heroin drug addicts, reducing the phobic component of craving by interacting with the Locus Coeruleus but has no effect on the pathways involved with positive reinforcement (13,14).

**Methadone**

The cornerstone in heroin dependence treatment is long term medication with opioid agonists, methadone, which have the greatest anticraving effect and create tolerance to narcotic action. Methadone's anticraving effect is not only due to its action on withdrawal symptoms nor to blocking the pharmacological effects of heroin, but more specifically to its action on the positive reinforcement mechanism.

Antagonist drugs block the euphoric effects of heroin, prevent tolerance and thus withdrawal yet addicts treated with antagonists have a kind of craving that manifests as dysphoretic mood and discomfort which frequently leads to interrupting treatment and relapsing to heroin use.

There are 3 possible treatment dosages with Methadone:

1. Withdrawal syndrome dosage (30mg/daily) which does not block opioid receptors and does not prevent relapses.
2. Blocking dosage. Euphoria is not experienced with heroin (60-80mg), although in this phase the subject may continue drug use. Drug seeking behavior may persist and the subject may use BDZ or alcohol to feel the effects of heroin.
3. Anticraving dosage (80-120 mg/daily) blocks craving which is at the base of drug seeking behavior (15).

The effective dosage capable of blocking opioid receptors is relatively constant whereas the anti-craving dose is more subjective. There is no pre-established anticraving limit and clinical evidence reports of subjects who experienced this limit at much higher dosages. We had one case of heroin drug addiction treated with three hundred and eighty mg of methadone daily.

Concurrent psychic or social factors may also contribute. Craving is observed when drug free subjects talk about heroin in group therapy or when they returned to areas where they had previously used drugs (so called reflex abstinence). It is also experienced