

People with opioid dependence in recovery show 're-regulation' of reward systems

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Within a few months after drug withdrawal, patients in recovery from dependence on prescription pain medications may show signs that the body's natural reward systems are normalizing, reports a study in the *Journal of Addiction Medicine*, the official journal of the American Society of Addiction Medicine.

The study by Scott C. Bunce, PhD, of Penn State University College of Medicine, Hershey, and colleagues provides evidence of "physiological re-regulation" of disrupted brain and hormonal responses to pleasurable stimuli—both drug- and nondrug-related.

Signs of Reward System Disruption After Drug Withdrawal...

The pilot study included two groups of seven patients in residential treatment for dependence on opioid pain medications. One group had recently gone through medically assisted opioid withdrawal—within the past one to two weeks. The other group was in extended care, and had been drug-free for two to three months. A group of normal controls were studied for comparison.

The researchers performed several tests to assess changes in the "[brain reward](#) system" during early recovery. After drug withdrawal, many people with opioid dependence have "persistent changes in the reward and memory circuits"—they may experience heightened "rewards" or

"pleasure" in response to drugs and related stimuli, but greatly reduced responses to naturally pleasurable stimuli (such as good food, or friendship).

Dr Bunce explains, "This is thought to occur because opiates are potent stimulators of the brain's reward system; over time, the brain adapts to the high level of stimulation provided by opiates, and naturally rewarding stimuli can't measure up." Such dysregulation of the natural reward system may contribute to the high risk of relapse during recovery.

The test results showed several significant differences in the reward system between groups. A test of startle reflexes showed that patients with recent drug withdrawal had reduced pleasure responses to "natural reward" stimuli—for example, pictures of appetizing foods or people having fun.

In brain activity studies, patients with recent drug withdrawal showed heightened responses to drug-related cues, such as pictures of pills. In the extended-care patients, these increased responses to drug cues—in a region of the brain called the prefrontal cortex, involved in attention and self-control —were significantly reduced.

...May Lead to New Objective Measures of Recovery

Patients who had recently withdrawn from opiates also had high levels of the stress hormone cortisol (adrenaline). In the patients who had been drug-free for a few months, cortisol levels were somewhat reduced, although not quite as low as in healthy controls. The recently withdrawn group also had pronounced sleep disturbances, while sleep in the extended care group was similar to controls.

All of these changes—brain and hormonal responses to drug cues and

natural rewards, as well as sleep disturbances—were correlated with abstinence time. The more days since the patient used drugs, the lower the abnormal responses.

The study supports past research showing dysregulation of the reward system during early recovery from opioid dependence. It also provides evidence that these responses may become re-regulated during several weeks in residential treatment—a period of "clinically documented" abstinence from opioids.

That's a potentially important step forward in [addiction medicine](#) research, Dr Bunce believes. "It shows that if the patient remains in treatment and off drugs for several months, the body's natural reward systems may have the capacity to return toward normal, making it easier for them to remain drug-free outside the treatment setting." With further study, tests of the natural reward system might provide useful, objective markers of recovery—clinical tests that help to evaluate how the patient's recovery is proceeding.

Such tests might help in managing the difficult problem of prescription [opioid dependence](#)—an ongoing epidemic associated with a high risk of relapse after drug withdrawal. Dr Bunce and colleagues are conducting a follow-up study, funded by the National Institute on Drug Abuse, to determine whether measures of the brain's [reward system](#), sleep and the stress response system indicate the capacity for re-regulation and the patient's risk of relapse during recovery.

More information: "Possible Evidence for Re-regulation of HPA Axis and Brain Reward Systems Over Time in Treatment in Prescription Opioid-Dependent Patients" [journals.lww.com/journaladdict ...
_HPA_Axis.99719.aspx](http://journals.lww.com/journaladdict..._HPA_Axis.99719.aspx)

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