

How dopamine drives cocaine craving

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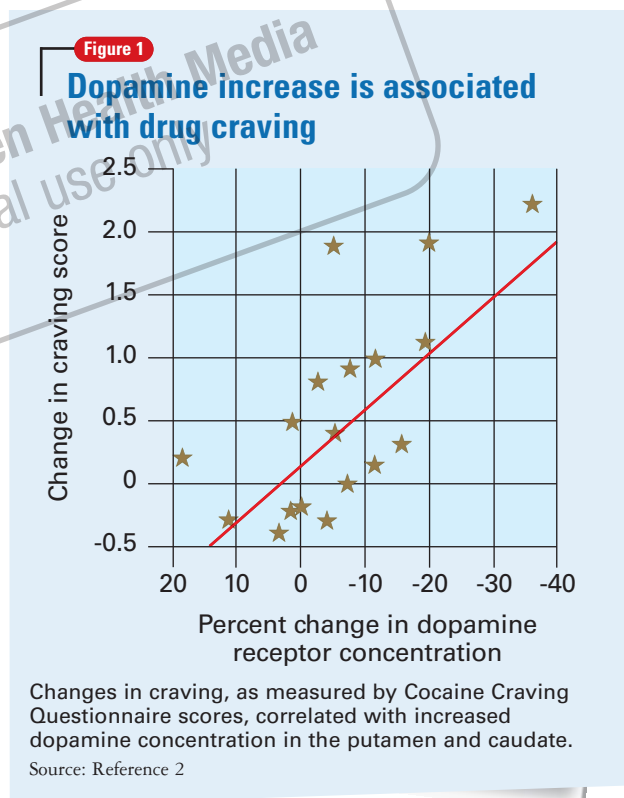
Fighting cravings' intense desire and obsessive thinking may be an addict's most formidable challenge.¹ Patients in recovery—desperate to stop abusing the substance—cannot control themselves after the craving is triggered. Remarkably, even after years of abstinence, cues reminding the addict of the substance—smells, sounds, or familiar surroundings—can ignite cravings and lead to relapse.

DOPAMINE AND DOPE

A recent imaging study suggests that dopamine may be the culprit behind cravings. Research with cocaine and rodents suggests that dopamine released in the dorsal striatum is associated with drug-seeking behavior. Measuring craving in a rodent is impossible, but a recent imaging study examined how drug cues affect the brains of drug-addicted humans (*Figure 1*).²

Volkow et al² injected 18 cocaine-addicted patients with a dopamine D₂ ligand that competes with endogenous dopamine and can be seen on positron emission tomography (PET). PET scans were then taken while each patient viewed a video of nature scenery (control) and then while watching scenes of drug preparation and simulated crack cocaine smoking.

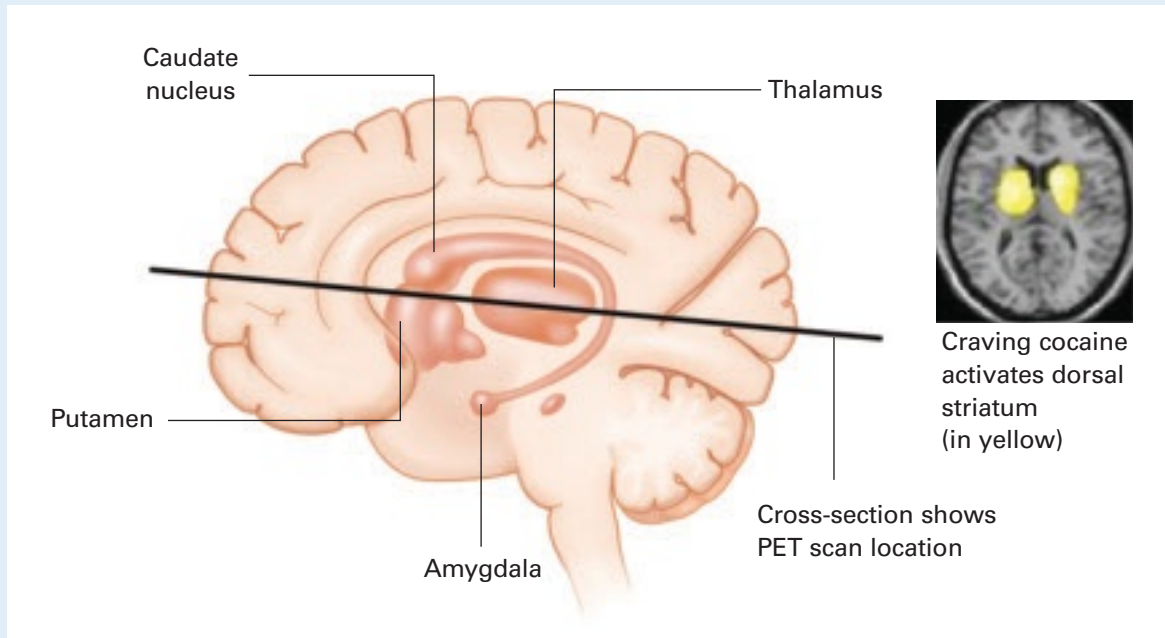
When the control scan was subtracted from the cocaine-cued scan, the dorsal striatum—activated by the cocaine preparation cues—stood out (*Figure 2*), suggesting the neurobiological mechanisms responsible for craving.



The dorsal striatum is thought to be involved with selecting and initiating actions. In this study, the cocaine video caused a release of dopamine into the dorsal striatum and a desire for the drug. In an earlier study, hungry subjects who were shown food cues also showed increased dopamine activity in the dorsal striatum in association with a desire for food.³

Figure 2

Dopamine release in the dorsal striatum is linked with craving



When cocaine-addicted patients watched a video depicting drug preparation and simulated crack cocaine smoking, PET scans of their brains showed dopamine release in the dorsal striatum.

Source: Reference 2

Taken together, these studies suggest that dopamine in the dorsal striatum mediates craving for a desired object. The primary source of this neurotransmitter in the dorsal striatum is dopamine cells in the substantia nigra. The visual stimulus must activate these neurons in the substantia nigra to induce craving.

CAVING INTO CRAVINGS

Desire precedes action and motivates behavior necessary for survival. Cocaine addiction apparently usurps the neurobiological mechanisms that motivate individuals to seek sustenance.

Developing an effective treatment for cocaine craving is a high priority at the National Institute on Drug Abuse.⁴ Medications including modafinil, propranolol, and disulfiram have been

found effective for cocaine addiction in randomized, controlled trials, although none are FDA-approved for this use.⁴

One could speculate that antipsychotics—which are potent dopamine receptor blockers—might calm the cravings associated with cocaine addiction. Unfortunately, it is not that simple. Older antipsychotics might increase substance use in patients with schizophrenia and substance abuse.⁵ However, compelling evidence suggests that clozapine can reduce drug and alcohol use in dually diagnosed patients with schizophrenia.⁶ This provides some hope that the newer antipsychotic medications could provide a broad spectrum of pharmacologic activity that has the capacity to cool off cravings that stimulate drug-seeking behavior.

continued

DRUG BRAND NAMES

Clozapine • Clozaril Modafinil • Provigil
 Disulfiram • Antabuse Propranolol • Inderal

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