Role of Dopamine, the Frontal Cortex and Memory Circuits in Drug Addiction: Insight from Imaging Studies-Part 2

Abstract: Dopamine is a chemical messenger in the brain. It is important in the brain reward system. Dopamine also plays a role in drug addiction. Drug addiction is a disease characterized by drug-induced "highs", withdrawal, and craving.

Many researchers use PET (positron emission tomography) images of the brain to study drug addiction. PET helps us to learn more about the role of dopamine and the brain pathways it controls.

PET scans show that increases in dopamine occur during drug use. Dopamines causes drug-induced highs. During withdrawal, PET scans show a decline in dopamine. Low dopamine reduces the good feelings from taking drugs. This will cause drug-seeking as a means to experience the high again. It may also cause the uncomfortable moods or cravings of withdrawal.

Using PET scans, we claim that changes in Dopamine levels help cause addiction. Dopamine disrupts parts of the brain that control motivation, drive and self-control.

Background: Dopamine, a chemical messenger in the brain, has many functions. It is important in behavior, thought, movement, motivation, reward, mood, sleep, attention, and learning. Dopamine activates some neurons. Dopamine sometimes attaches to proteins called dopamine receptors and dopamine transporters (DAT). This lowers levels of dopamine in the brain. *When dopamine can't attach to the proteins, dopamine levels in the brain rise.*

Images of the human brain in action allow expanded drug addiction research. These images are created by PET scans. PET scans allow researchers to see areas of brain activity during specific events. This has helped understand brain pathways and addiction. PET scans allow scientists to see how dopamine affects brain circuits.

Addiction pathways in the brain are formed during drug-induced highs. These highs feel good and the brain remembers what caused the good feelings. Drug users want to repeat experiences that feel good. Soon, more and more of the drug is needed to get the same good feeling. Withdrawal results when the drug is no longer taken. This is followed by a powerful desire for the drug (craving). Craving leads to repeated use of drugs of abuse. In turn, repeated drug use strengthens addiction pathways in the brain.

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AUTHORS:
Nora D. Volkow,*
Joanna S. Fowler,†
Gene-Jack Wang,* and
Rita Z Goldstein*
*Medical Department and Chemistry Department, Brookhaven National Laboratory, Upton, New York 11973

All learned behaviors make specific pathways in the brain. These pathways create long-term memories. Brain pathways can change in strength. Strengthening brain pathways helps us to learn and remember things. In this way, addiction becomes a life-long disease.

Methods: This article is a review of over 77 studies. Review articles are useful in pulling together the results of many studies and providing a "current state" of research. This type of effort is especially helpful in rapidly expanding areas of research. The authors of this paper divided the review into five specific areas of drug addiction research; one is included below.

RESULTS AND SUMMARIES OF RESEARCH:

Dopamine Involvement in Drug-Induced Highs

A. Cravings in drug abusers -
We measured changes in dopamine caused by the drug MP. Compared with controls, cocaine abusers had:

a. Lowered levels of dopamine (50% lower) (Volkow et al., 1997)
b. Less intense highs
c. Abnormal, high responses in the thalamus of the brain when they had cravings (this did not occur in control subjects) (Volkow et al., 2000)

An unexpected finding occurred in this area of research. Researchers used to think that a stronger reward when taking drugs caused cravings in addicted people. Instead, cravings may be caused by an abnormal response in the thalamus of drug abusers. The surprise finding paves the way for more studies into how the thalamus may cause drug cravings.

B. Reward circuits less sensitive in drug abusers (more and more drug is needed to achieve a "high") - PET studies found that addicts have fewer dopamine receptor proteins (***Table 1 and Figure 3***). Fewer receptor proteins causes more brain dopamine. Over time, more dopamine causes the reward circuits of drug abusers to be less sensitive. As the reward circuits become less sensitive, more of the drug is required to feel high (Volkow et al., 2000).

TABLE 1 Dopamine Receptor Availability* in Controls and in Drug Abusers

	Controls	*Abusers*
Alcoholics	2.71 (*n* = 17)	2.10 (*n* = 10)
Heroin abusers	2.97 (*n* = 11)	2.44 (*n* = 11)
Cocaine abusers	2.90 (*n* = 23)	2.59 (*n* = 20)
METH abusers	2.81 (*n* = 20)	2.45 (*n* = 15)

Note: Dopamine Receptor Availability is measured in Bmax/Kd

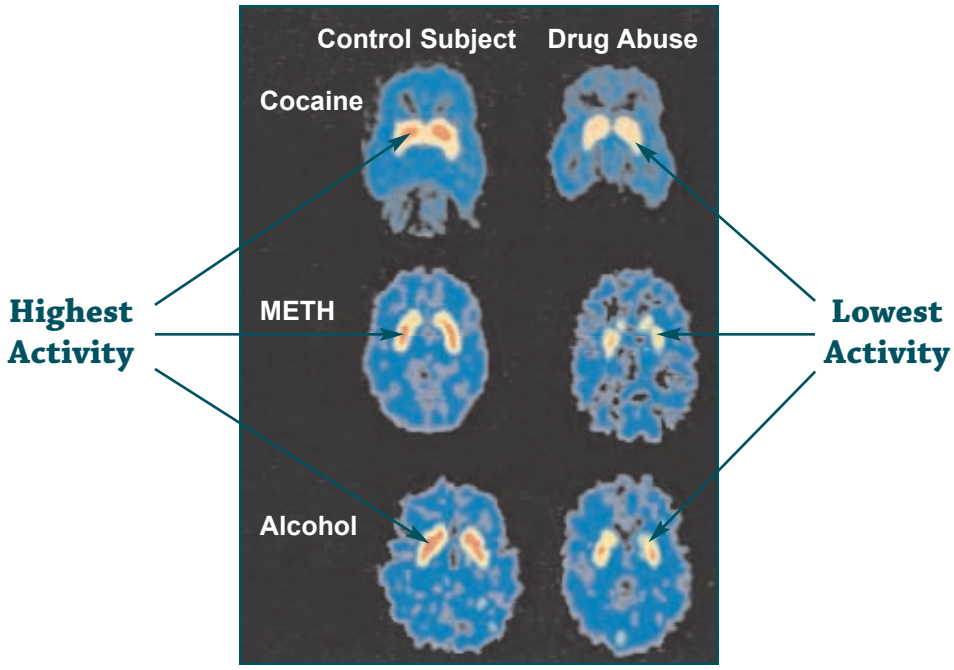

Figure 3 Brain Images of Dopamine Receptors in Brains of Control Subjects and Drug Abusers

C. Detoxified Drug Abusers **-** In several PET scan studies of detoxified drug users, two parts of the brain that control motivation, reward, habits, and emotions were activated. This is important information (Tucker et al., 1995; Insel, 1992; Rolls, 2000; Schultz et al., 2000; Devinsky et al., 1995). It shows that brain-based changes cause addictive behavior, including craving, withdrawal, and drug seeking.

Conclusion: Imaging studies show drug-addicted brains have major problems with dopamine function. These problems, in turn cause changes in brain pathways involved in reward, motivation, memory, drive, judgment, and self-control. Drug addiction is a long-term disease caused by long-term biological changes.

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