Role of Dopamine, the Frontal Cortex and Memory Circuits in Drug Addiction: Insight from Imaging Studies-Part 1

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. Dopamine 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.

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.

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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

In one study, a group of cocaine abusers received cocaine. Another group of healthy control subjects received another drug called MP. MP acts like cocaine, but is not addictive. Both cocaine and MP raise levels of dopamine in the brain (Ritz et al., 1987). They raise dopamine by attaching to dopamine transporters (DAT). DATs are proteins that normally bind to dopamine, clearing it from neurons. If drugs like cocaine and MP bind to the DATs instead, dopamine floats freely, *causing levels of dopamine to rise higher than normal* (Ritz et al., 1987).

Cocaine and MP occupied more than 60% of DATs. This caused more dopamine in the brains of test subjects (Volkow et al., 1994). Test subjects generally reported feeling high as dopamine levels in their brains increased (Figure 1).

There was, however, an unexpected finding in this study! Some test subjects did not feel high even when 50% of DAT were occupied by the cocaine and MP (see ***Figure 1***). This unexpected result was an *opportunity* to extend the research. We formed a new hypothesis to explain why the drug did not cause a high in some test subjects. Maybe there is another protein to which the drug can bind.

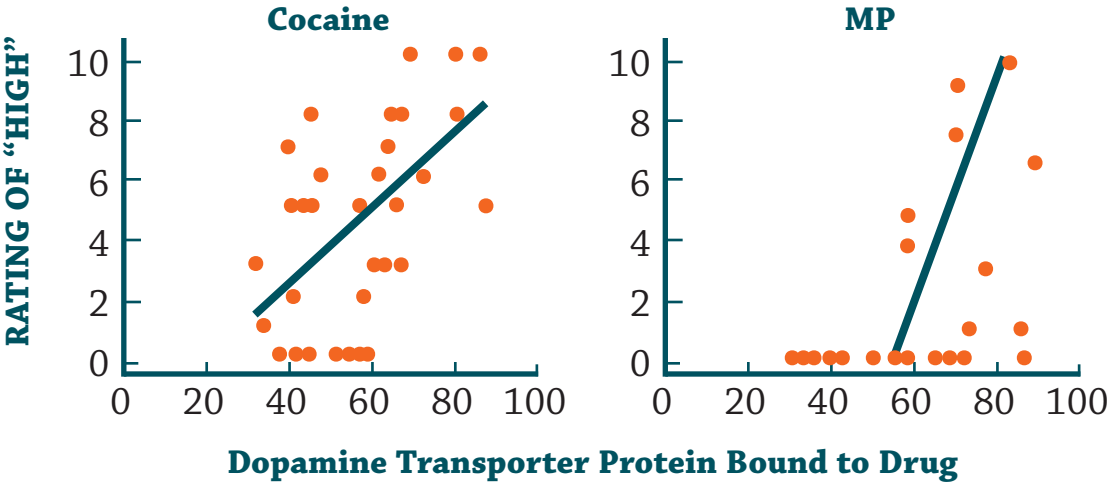

Figure 1 Rating of Drug-Induced High vs Percentage of Dopamine Transporter Binding

Note: When dopamine can't attach to the dopamine transporter protein because the drug attached to it, dopamine levels rise.

We designed a new study to test the new hypothesis. Healthy test subjects were given the drug MP. We did brain PET scans. This time, however, the drug attached to a dopamine *receptor* protein (instead of a transporter protein). *This is another way in which dopamine levels rise in the brain.* Dopamine levels increased in more test subjects this time. They reported feeling high as dopamine increased in their brains. When dopamine did not increase, test subjects did not feel high (***Figure 2***). Researchers found a second way for dopamine levels to rise. Increases in dopamine were again linked to feeling high.

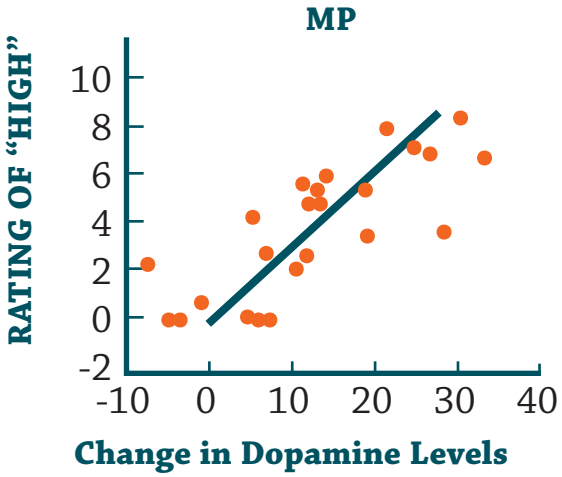

Figure 2 Rating of Drug-Induced High vs Change in Dopamine Levels When MP Drug is Taken

Fischman and Foltin (1991) reported the same results. Therefore, two independent studies had the same findings.

Conclusion: Imaging studies show drug-addicted brains have major problems with dopamine function. Researchers have found two ways in which dopamine levels in the brain are controlled. If drugs of abuse bind to either transporter receptor proteins, dopamine levels in the brain rise. The result is feeling high. Dopamine is important in the addiction process.

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