

Sleep Deprived? Mind your dopamine.

By [Scicurious](#) | June 4, 2012

Most of us will suffer sleep deprivation at one time or another. I'm not talking our usual state of broken sleep, 5 hours a night, or something else. **I'm talking a full night without sleep**, the kind many people experience in the army, with a brand new (or not so brand new) baby, or more frivolously (I hope), in college.

We all know **what sleep deprivation does to us**. We're unable to pay attention. We're often cold or hot. We can't think straight, we start doing very strange things (you would not BELIEVE the crazy dances I've made up...), and of course, we're really, really tired.

But why do these symptoms happen? **What's going on in the brain during sleep deprivation to explain this behavior?** Well, in part, **it might be changes in your D2 receptors (down-regulation of dopamine receptors)**. Volkow et al. "Evidence That Sleep Deprivation Downregulates Dopamine D2R in Ventral Striatum in the Human Brain" Journal of Neuroscience, 2012.

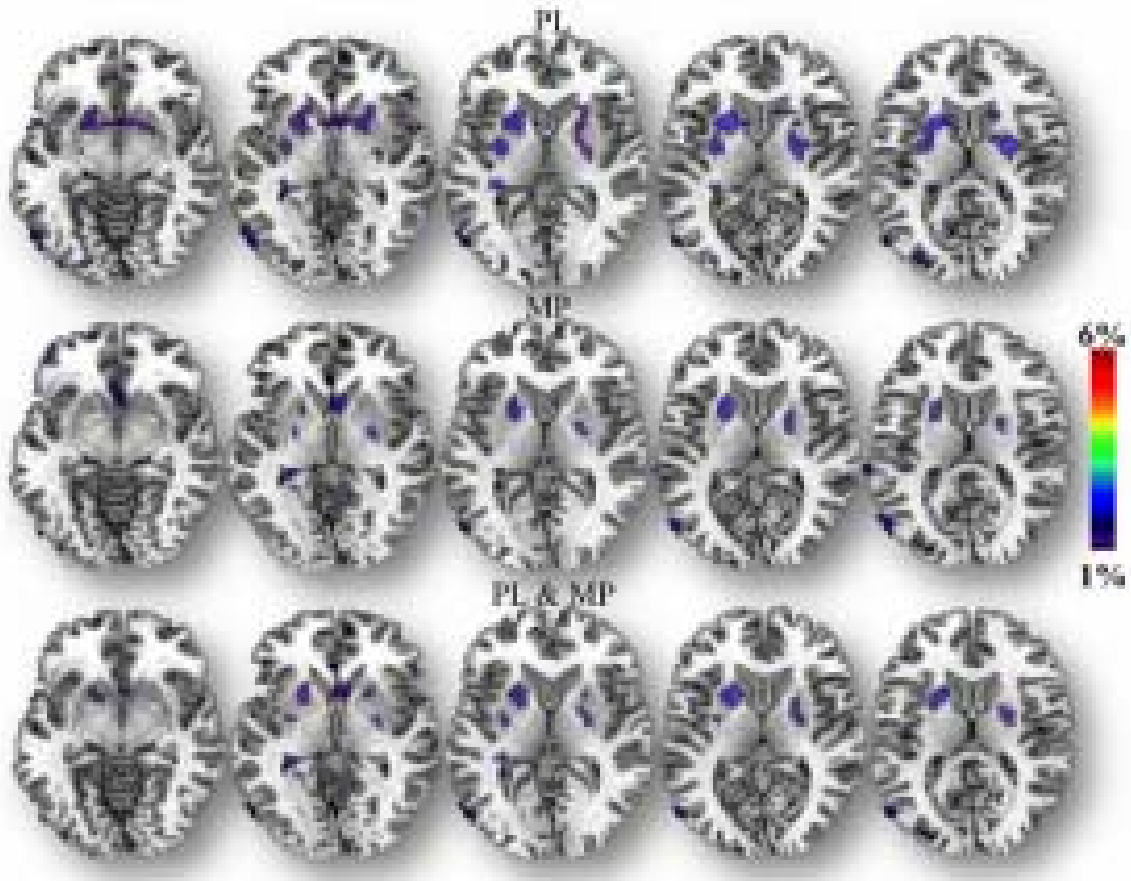
There are lots of signs that point toward the **involvement of the neurotransmitter dopamine in wakefulness**. Drugs that increase levels of dopamine in brain (including, but not limited to, drugs like **cocaine, amphetamine, meth, and Ritalin**) also increase feelings of wakefulness. Increasing dopamine in the brain via genetic alterations, like getting rid of the dopamine transporter in a mouse, stopping dopamine from getting recycled, produces a mouse that sleeps less. **Diseases that are characterized by low dopamine levels, like Parkinsons, also have daytime sleepiness.**

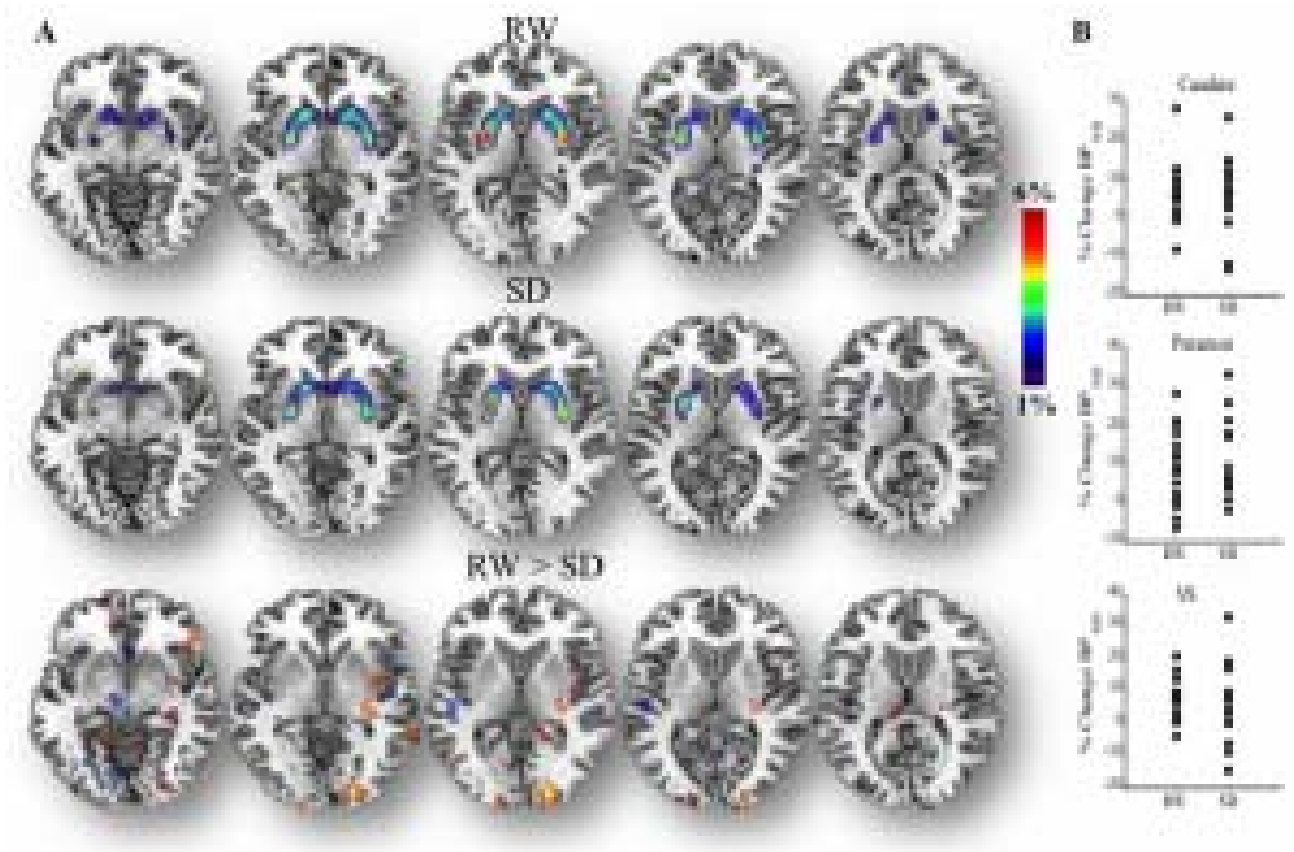
But a **neurotransmitter is only as good as its receptor**. Dopamine has **two main types of receptors**, and the current hypothesis is that the **wakefulness promoting effects of dopamine may be controlled partially by the D2 type receptor**. Antipsychotics, which **block D2 type receptors, make people sleepy**, and previous studies showed decreased D2 binding in the brains of sleep deprived people. But the question is: what is causing the decreases in D2 when people are sleep deprived? The *authors of this study hypothesized that this was due to increased dopamine release*, which would cause decreases in D2 receptors (**this is a basic idea in pharmacology, when a group of receptors is overstimulated, some receptors will leave the membrane, making the membrane less sensitive to stimulation**).

To test this hypothesis, they took a bunch of human volunteers, and either sleep deprived them overnight (they kept them in a facility with a nurse bugging them to keep their eyes open if they got drowsy), or kept them in the facility to get a good night's rest (all participants underwent both conditions). In the morning, they looked at the D2 receptors in the striatum of the brain, an area with loads of dopamine and associated with things

like arousal and reward. To do this, they used positron emission tomography (PET), which uses a radioactive tracer (C-raclopride), which binds to D2 type receptors, allowing you to see how many are present.

They showed that D2 type receptor binding was definitely lower in sleep deprived people. But what does this mean? Does it mean that there's more dopamine release when you're tired, decreasing the D2 type receptors? Or do the D2 type receptors decrease for some other reason? To look at this, the authors of the study treated the participants with methylphenidate (Ritalin), which increased the amounts of dopamine. They hypothesized that if sleep deprivation produced more dopamine release, the methylphenidate should produce larger increases in dopamine than in well rested patients.





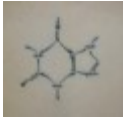
Above you can see nice pretty pictures showing places where the methylphenidate produced larger or smaller changes in sleep deprived patients vs not...but overall there was no difference.

This means that the **decrease in D2 type receptors that the authors see with sleep deprivation is NOT due to increases in DA release during sleep deprivation.** They confirmed this with studies in rats, and **showed that the sleep deprived rats showed no increases in dopamine, but showed similar D2 type receptor changes.**

So what is going on? Unfortunately, the authors didn't go after that question, though they talk about a "different physiological mechanism". They do *hypothesize that adenosine might have something to do with it. Adenosine is a neurochemical which you know best from your morning cup of coffee. Caffeine increases wakefulness by antagonizing adenosine receptors, and adenosine itself promotes sleepiness.* Not only that, one of the **areas involved in this effect appears to be the striatum**, the dopamine-rich area the authors were looking at in this study. **Caffeine can increase D2 type receptor levels in this area.** So it seems like the next thing to look at would be how adenosine and dopamine might be interacting following sleep deprivation (though unfortunately, they didn't look at it here).

So what does this mean? Well, **the changes in D2 type receptors could help explain some of the other changes in behavior that come with sleep deprivation, changes like increases in risk taking behavior, impulsivity, and drug relapse.** These are all things which increase when people are sleep deprived. *So the changes seen in D2 type receptors could help explain show these behavioral changes occur. But while we see changes in receptors, we still don't know why, and the proposed mechanism still needs to be tested.*

Volkow, N., Tomasi, D., Wang, G., Telang, F., Fowler, J., Logan, J., Benveniste, H., Kim, R., Thanos, P., & Ferre, S. (2012). Evidence That Sleep Deprivation Downregulates Dopamine D2R in Ventral Striatum in the Human Brain *Journal of Neuroscience*, 32 (19), 6711-6717 DOI: [10.1523/JNEUROSCI.0045-12.2012](https://doi.org/10.1523/JNEUROSCI.0045-12.2012)



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