



From the editor

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Pathways of pleasure and pain

How well do you know dopamine?

There is much more to dopamine than schizophrenia and Parkinson's disease. Research has discovered a fascinating array of dopamine functions, some as triggers for neuropsychiatric disorders and others critical for healthy living.

Here's a quiz; how many of the following functions of dopamine's six receptors and four pathways do you know?

Motor coordination. Most of us take for granted moving or handling objects, thanks to normal dopamine levels in our nigrostriatal tracts. However, one look at a person afflicted with Parkinson's disease trying to walk or hold a cup of coffee should make us grateful to dopamine for freedom of movement.

Abnormal vs. reality testing. Normal dopamine activity in the mesolimbic tract is vital to maintaining a healthy, adaptive awareness of our surroundings. Persons with abnormally heightened dopamine activity in the medial temporal region—for example, abusers of dopamine agonists such as methamphetamine (*see page 46*)—can be tormented by ideas of reference and delusions about neutral environmental stimuli.

Reward and pleasure. It is hard to imagine life without experiencing fun doing pleasurable activities. So

give credit to dopamine in the ventral striatum for all the activities you enjoy, such as playing golf, watching an opera, or socializing with good friends. The dopamine receptor gene has been referred to as “the reward gene.”

Cognition and decision-making. Critical cognitive tasks such as memory, attention, and executive functions depend on an intact mesocortical dopamine pathway. Going to school or holding a job is impossible if mesocortical dopamine is deficient, which is why persons with schizophrenia become disabled.

Give credit to dopamine in the ventral striatum for all the activities you enjoy

Placebo effect. Psychiatrists appreciate the high placebo response rates associated with treating depression, anxiety, insomnia, or pain. Research implicates the release of dopamine in the reward pathways that probably are involved in alleviating psychiatric and physical symptoms. Even patients with Parkinson's disease receiving sham deep brain stimulation or striatal tissue transplants in controlled clinical trials may improve initially because of dopamine release.

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Depression. Dopamine is a monoamine that modulates mood, and a decrement in dopamine leads to dysphoria or major depression. Dopamine deficiency states such as Parkinson's disease are frequently

When L-dopa was first used in parkinsonism, one side effect was increased sexual drive

associated with depression and can be treated with dopaminergic antidepressants.

Social defeat. People—and animals as well—can develop permanent aversion to social contact if exposed to unrelenting abuse and violence. Mesolimbic dopamine pathways are implicated in this syndrome of “social defeat,” which can be reversed by chronic administration of antidepressants.

Alcohol dependence. Dopamine receptor dysfunction has been linked with a propensity to abuse alcohol and to reduced sensitivity to reward. The mesolimbic dopamine pathway appears to be critical for experiencing pleasure from abused drugs and is thought to be a common denominator for addictions and drug-seeking behavior.

Hypersexuality. When levodopa [L-dopa] was first used to treat Parkinson's disease, one of its earliest side effects was increased sexual drive. This effect has been observed with other dopamine agonists and is attributed to potentiation of reward pathways that reinforce pleasurable activities. Other factors also may be involved, as in impulse control disorders.

Pathologic gambling. Treating Parkinson's disease with dopamine agonists has been associated with an increase in pathologic gambling, an impulse control disorder. The incidence approaches 10%.

Compulsive shopping. Excessive, inappropriate buying is another impulse control disorder that emerges during dopamine agonist therapy.

ADHD. A cortical/frontal dopamine deficit is believed important in the pathophysiology of attention-deficit/hyperactivity disorder. ADHD symptoms can be alleviated with dopamine agonists (stimulants).

Dopamine can enhance health but also disrupt movement, mood, and behavior and lead to neuropsychiatric disorders. This neurotransmitter can reward or torment us. I invite you to send me e-mail (henry.nasrallah@currentpsychiatry.com) to comment on the 12 functions I've listed above or on other disorders you have observed that result from excessive or deficient dopamine activity.



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P.S. Three days after I wrote this editorial, researchers announced another potential role for dopamine: regulating the sleep-wake cycle.¹ Excess dopamine in mice allowed rapid-eye movement (REM) sleep (i.e., dreaming) to intrude on wakefulness! This may explain the dreamlike hallucinations in schizophrenia or L-dopa psychosis. Mice with depleted dopamine stopped having REM, even during sleep, but injecting them with D2 receptor agonists restored REM.

Reference

1. Dzirasa K, Ribeiro S, Costa R, et al. Dopaminergic control of sleep-wake states. *J Neurosci* 2006 Oct. 11;26:10577-89.

SCORE YOURSELF

How many of these 12 dopamine functions did you know?

1 to 3 = **Fair**; 4 to 6 = **Good**; 7 to 9 = **Very Good**; 10 to 13 = **Outstanding**