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"Magic" pills

The mechanics of antipsychotic medications

Caitlin Crawshaw

It seems ironic that such life-altering symptoms as hallucinations, delusions, or disorganized thinking can be eased with just a small, white pill. For people with schizophrenia though, the right pharmaceutical treatment in the right dosage means the difference between a runaway mind and peace.

As mysterious as the medication can seem, there's no magic here—just a whole lot of science. Here's a layperson's guide to how drugs work their "magic" inside your body.

Dopamine and schizophrenia

Although its symptoms can have psychological impacts (like social isolation and depression), schizophrenia is fundamentally a neurological disorder.

Compared with most people's brains, those with schizophrenia have imbalances of dopamine—an important chemical messenger—in two parts of the brain, explains Joe Wegmann, PD, LCSW, a New Orleans pharmacologist and therapist.

In the limbic system, which regulates mood, affect, and to a lesser extent, cognition, there's too much dopamine, creating "the classical psychotic symptoms" like hallucinations and delusions, Wegmann says. In the pre-frontal cortex, however, there's actually a shortage of dopamine, which creates the negative symptoms associated with schizophrenia, such as apathy and anhedonia (difficulty experiencing pleasure).

"The key is to develop a medication that deactivates limbic dopamine—so the delusions, hallucinations, and disorganization begins to improve—but activates it in the cortical system," says Wegmann.

Unfortunately, half a century after the first generation of antipsychotics emerged, he says drugs for schizophrenia continue to only treat the excess of dopamine in the limbic system. "It's very difficult to create a drug molecule that has to perform two functions."

To compensate, clinicians often prescribe other medications, like antidepressants and antianxiety medications, to try to restore the motivation that many people lose after they develop schizophrenia. It has little effect, though, says Wegmann, since these drugs are "fighting the headwind of the psychotic features."

Though these additional medications may have some benefits to people with schizophrenia, they rarely have a big impact, he argues: "It's like trying to walk directly into a 50 MPH gale wind. You can only take maybe a few steps at a time."

Drug delivery systems and you

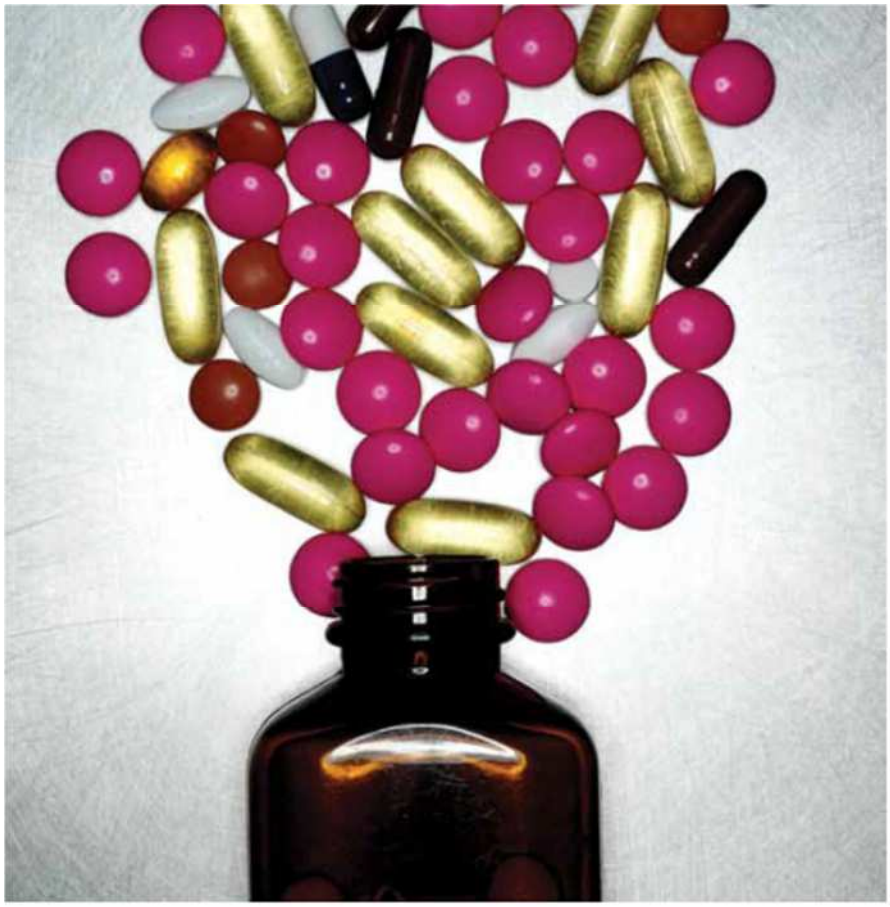
Like any other medication, antipsychotics can be delivered a plethora of ways. Some people swallow a small pill at regular intervals. Others may place a quick-dissolving tab under the tongue. There are also long-acting injectables (LAIs) which are administered with a needle into body tissues, allowing the drug to be absorbed very slowly and used by the brain as needed. For people who struggle to take their medications regularly or are non-compliant, LAIs offer the chance to get a shot every few weeks and avoid the daily medicine regimen.

Regardless of how you take an antipsychotic—whether as a pill or an injection—it works exactly the same once it's absorbed into your body, explains Donald Addington, MD, the chair of the Canadian Psychiatric Association. However, pills that are swallowed will naturally move into the stomach, intestines, and are metabolized in the liver, where much of the drug can be destroyed. "The liver is the clean-up factory," he explains. Those drugs that are injected into the body bypass the digestive system and can make their way to the brain directly.

Journey through the body

Once the medication has been absorbed into the body—whether via the stomach and liver or through injection into bodily tissues—it must travel through the bloodstream to the brain where it will do its work. But before these molecules can reach the brain, they move through the blood-brain barrier, made up of endothelial cells, which block microscopic particles. Since drug molecules are tiny, they are able to pass through to the other side.

Once in the brain, all antipsychotic medications seek out the limbic system, a set of brain structures that includes the hippocampus, amygdala, anterior thalamic nuclei, septum, and limbic cortex. Here, the antipsychotic drug molecules will gravitate to the dopamine neurotransmitters which are being produced in excess.



Attached to every neurotransmitter is a receptor, which acts like a keyhole in a door, says Addington. Some drugs (like antipsychotics) bind with a receptor, much like an ill-fitting key fits into a lock but can only block the light, not open a door. "It's as though you were having less of the neurotransmitter, because some of the receivers are blocked," he explains. When a receptor and molecule are stuck together, the neurotransmitter is disabled.

Complications

Once in the bloodstream, there's little to prevent a drug molecule from making its way to the brain and doing what it was designed to do. However, before the drug is absorbed into the blood stream, it's usually processed by the liver, which acts as the body's gatekeeper.

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This is where a drug's work may be hindered. If the liver has been damaged, and the drug isn't metabolized properly, it may build up in the body in unhealthy concentrations. The same can happen if a person is consuming too much alcohol, says Wegmann. Excess levels of a drug can be toxic and with some drugs, regular blood-testing is performed to ensure a person has a normal level of the drug in their system.

No one-drug-fits-all solution

The process by which antipsychotic drugs do their work in the body is the same for everyone, but how well the drug works depends on individual differences. The extent to which these receptors and molecules bind together depends on a person's genetic makeup, says Addington.

Coffee drinkers provide a useful analogy, he explains. While some people can have a cup before bed and fall asleep the moment their cheek hits the pillow, others are tossing and turning if they have a cup after lunchtime. Even if two people have consumed the exact amount of coffee in the same concentration, their body will process it differently.

The same holds true with schizophrenia medications, which is why it's not uncommon for people to try a couple before finding the right fit. While no one knows exactly why people with schizophrenia are more responsive to some medications than others, it could be because people have different proportions of receptors in their brains, says Addington.

These genetic differences can make prescribing challenging for clinicians, since "there's no recipe here; there's no formula," as Wegmann puts it. Matching a patient with the right medication—and the right dose of that medication—is still trial and error.

The future of antipsychotics

Unfortunately, there are no pharmaceutical options to help with negative symptoms like diminished motivation, says Wegmann. "Schizophrenia is very mysterious and this is going to take years to unravel," he says, noting it could take decades for a treatment that addresses dopamine imbalances in both parts of the brain.

The good news is that delivery options continue to expand. More drugs are being offered as LAIs or dissolvable tablets, allowing for greater treatment options in emergency situations and for people who struggle to take their medication consistently.

There are also more varieties of second-generation antipsychotics on the market, offering people a greater chance of finding a drug that's conducive to their unique body chemistry, says Wegmann. Recent releases include Latuda (late 2010) and Saphris (2009). ★