BODY·MIND·SPIRIT

THE CHEMICAL CURE: THE SUCCESSES OF PSYCHOPHARMACOLOGY

BY BETTINA MARKS

Had Prozac been made available in previous centuries, folks such as Abraham Lincoln, Theodore Roosevelt, Robert Schumann, Ludwig von Beethoven, Edgar Allen Poe, Mark Twain, Vincent van Gogh and Georgia O'Keefe would probably all have been on a strict dosage. Each of them battled the debilitating illness of depression, a disease that affects people of all locations and cultures, particularly in this post-9/11 world.

According to the National Institute for Mental Health (NIMH), approximately 18.8 million American adults, or about 9.5 percent of the U.S. population age 18 and older in a given year, have a depressive disorder. Nearly twice as many women (12 percent) as men (6.6 percent) are affected by a depressive disorder each year. These figures translate to 12.4 million women and 6.4 million men in the United States.

Depression profoundly impairs the ability to function in everyday situations by affecting moods, thoughts, behaviors and physical well-being. Depression can range in intensity from mild to severe. An interaction between genetic tendency and life history appears to determine a person's chance of becoming depressed. Episodes of depression may be triggered by stress, difficult life events, side effects of medications, medication/substance withdrawal or even viral infections that affect the brain.

Evidence indicates depression stems from imbalances in the brain's neurotransmitters, the chemicals that allow communication between nerve cells. Serotonin and norepinephrine are two neuro-transmitters thought to play an especially important role. Since the discovery of serotonin in the 1950s, researchers are finding evidence that one of its roles is to mediate emotions and judgment. Along with dopamine, these three chemicals have to be present in proper levels to keep our emotions in balance.

Neurotransmitters act as chemical messengers that carry out communication in the brain and body. The message-molecules flow from a nerve cell or neuron into other neurons that act as receivers. There, they attach to a distinctly shaped area on the neuron called a receptor site. This union, like a key fitting into a lock, triggers signals that either allow the message to be passed on to other cells or prevent the message from being forwarded.

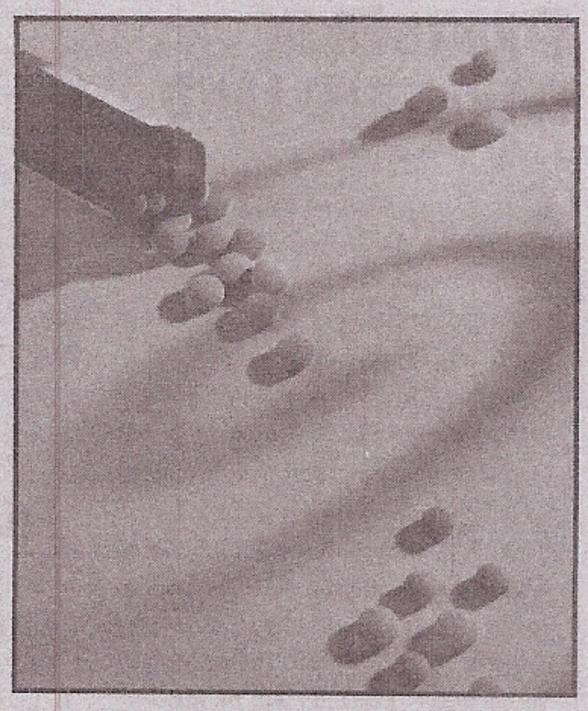
Dopamine is similar to adrenaline, and affects brain processes that control movement, emotional response and the ability to experience pleasure and pain. Dopamine binds to its receptors quickly. Regulation of dopamine plays a crucial role in our mental and physical health. Neurons containing the neurotransmitter dopamine are clustered in the midbrain in an area called the *substantia nigra*. This neurotransmitter is quickly removed from its receptors as long as dopamine levels in the synapse are sufficiently high.

Some drugs are known as dopamine agonists, binding to dopamine receptors in place of dopamine and directly stimulating those receptors. Some dopamine agonists are currently used to treat Parkinson's disease. In contrast to dopamine agonists, dopamine antagonists are drugs that bind but don't stimulate their receptors. Antagonists can prevent or reverse the actions of dopamine by keeping it from attaching to receptors. Dopamine antagonists are traditionally used to treat schizophrenia and related mental disorders.

Medications for mental illness were first introduced in the early 1950s. From the 1960s through the 1980s, tricyclic antidepressants (named for their chemical structure) were prescribed for major depression. Most of these medications targeted norepinephrine and serotonin issues. Though the tricyclics are as effective in treating depression as the newer antidepressants, their side effects are usually more unpleasant.

Other antidepressants introduced during this period were monoamine oxidase inhibitors (MAOIs). Naturally in the brain, MAO protects the "purity" of neurotransmission by breaking down other neurotransmitters. In a sick patient, inhibiting MAO can increase levels of neurotransmitters such as serotonin. This is the basis for the success of these drugs in treating depression. MAOIs are effective for some people with major depression who do not respond to other antidepressants.

In the past decade, newer antidepressants have been introduced that work as well as the older ones, but with fewer side effects. Some of these medications primarily affect serotonin and are called selective serotonin reuptake inhibitors (SSRIs). Prozac, which was introduced in 1988, is the most popular of this category. SSRIs are the primary treatment for depression today because experts believe they are safe and efficient. Prozac is one of the most widely prescribed antidepressants in the United States. and has been taken by over 12 million people worldwide. (Others in this category include Zoloft, Luvox, Paxil and Celexa.) SSRIs work by blocking the pre-synaptic serotonin transporter receptor. These vary in the potency and effect. In contrast to tricyclic antidepressants (TCAs), SSRIs are stronger inhibitors of serotonin reuptake.



Side effects from SSRIs include sexual problems, headache, nausea, nervousness, and insomnia and agitation. Any of these side effects may be amplified when an SSRI is combined with other medications that affect serotonin. In the most extreme cases, such a combination of medications (e.g., an SSRI and an MAOI) may result in a potentially serious or even fatal "serotonin syndrome," characterized by fever, confusion, muscle rigidity, and cardiac, liver or kidney problems.

In the later 1990s, newer medications were introduced, which, like the tricyclics, affect both norepinephrine and serotonin, but with fewer side effects. These new medications include Effexor and Serzone. Wellbutrin, Desyrel, Effexor and Remeron are a group of structurally unrelated antidepressants that don't fit into any of the established antidepressant drug classes. Wellbutrin affects dopamine, Desyrel affects serotonin, and Effexor affects norepinephrine, serotonin, and dopamine, while Remeron stimulates norepinephrine and serotonin release, blocking certain receptors. Wellbutrin, Effexor, Desyrel, and Remeron appear to cause fewer serious side effects than MAO inhibitors or tricyclics.

These newer medications can cause a few unusual problems in some people and no one is sure of their long-term effects. The biggest risk with Wellbutrin not found in other antidepressants is the possibility of seizures. There have been troubling reports that Effexor may cause tardive dyskinesia, a movement disorder that may be permanent, involving writhing, wormlike movements of the body, lips and tongue. The most common side effects shared by Wellbutrin, Effexor and Desyrel include agitation, dry mouth, insomnia, headache, nausea and vomiting, constipation and tremors.

Wellbutrin apparently works not unlike cocaine, which increases dopamine levels by preventing dopamine reuptake, leaving more dopamine in the synapse. Drugs such as cocaine and amphetamines produce their effects by changing the flow of neurotransmitters. These drugs are defined as indirect acting, because they depend on the activity of neurons. In contrast, some drugs bypass neurotransmitters altogether and act directly on receptors. Such drugs are called direct acting.

But with all this pharmaceutical culture, let's not forget there are natural ways of fighting depression. Serotonin levels can be stimulated by a multitude of activities, including walking, exercising, performing physical labor, climbing stairs, cleaning and having sex. Sometimes working up a good sweat can also be an effective fix for life's sometimes-unpleasant realities.