tiates a Grand Mal Attack? Most people who
mal attacks have a hereditary predisposition to
redisposition that occurs in about 1 of every 50
ns. In such people, factors that can increase the
of the abnormal "epileptogenic" circuitry enough
te attacks include (1) strong emotional stimuli,
caused by overbreathing, (3) drugs, (4) fever, and
ses or flashing
netically predisposed, cer-
ost any part of the brain
brain areas, as we dis-
ransmit signals into the
and mal seizures.

he cause of the
nd mal attack is
ivation of many
nout the brain.
attack after a few
is probably *active*
been activated by

involves the thalamo-
is usually characterized
sness (or diminished con-
the person has twitchlike
ly in the head region, espe-
is followed by return of con-
of previous activities. This total
*nce syndrome* or absence epilepsy.
such attack in many months or, in
a rapid series of attacks, one after
rse is for the petit mal attacks to
hildhood and then to disappear by
on, a petit mal epileptic attack will
k.
tern in petit mal epilepsy is dem-
le recording of Figure 59-5, which
*nd dome pattern*. The spike and
ver most or all of the cerebral
e involves much or most
tem of the brain. In
from oscillation
s (which are
producing
cortico-
2) *excitato*
ns.

n involve almost any local part of the brain,
regions of the cerebral cortex or deeper
the cerebrum and brain stem. Most often,
ılts from some localized organic lesion or
ıality, such as (1) scar tissue in the brain
djacent neuronal tissue, (2) a tumor that
of the brain, (3) a destroyed area of brain
ıitally deranged local circuitry.
these can promote extremely rapid dis-
neurons; when the discharge rate rises
lred per second, synchronous waves
adjacent cortical regions. These waves

gradually recruit
leptic discharge zone. The proc
at a rate as slow as a few millimeters a minute to
several centimeters per second. When such a wave of excl-
tation spreads over the motor cortex, it causes progressive
"march" of muscle contractions throughout the opposite side
of the body, beginning most characteristically in the mouth
region and marching progressively downward to the legs but
at other times marching in the opposite direction. This is
called *jacksonian epilepsy*.

A focal epileptic attack may remain confined to a single area of the brain, but in many instances, the strong signals from the convulsing cortex excite the mesencephalic portion of the brain-activating system so greatly that a grand mal epileptic attack ensues as well.

Another type of focal epilepsy is the so-called *psychomotor seizure*, which may cause (1) a short period of amnesia; (2) an attack of abnormal rage; (3) sudden anxiety, discomfort, or fear; and/or (4) a moment of incoherent speech or mumbling of some trite phrase. Sometimes the person cannot remember his or her activities during the attack, but at other times he or she is conscious of everything that he or she is doing but unable to control it. Attacks of this type frequently involve part of the limbic portion of the brain, such as the hippocampus, the amygdala, the septum, and/or portions of the temporal cortex.

The lowest tracing of Figure 59-5 demonstrates a typical EEG during a psychomotor seizure, showing a low-frequency rectangular wave with a frequency between 2 and 4 per second and with occasional superimposed 14-per-second waves.

**Surgical Excision of Epileptic Foci Can Often Prevent Seizures.** The EEG can be used to localize abnormal spiking waves originating in areas of organic brain disease that predispose to focal epileptic attacks. Once such a focal point is found, surgical excision of the focus frequently prevents future attacks.

## Psychotic Behavior and Dementia—Roles of Specific Neurotransmitter Systems

Clinical studies of patients with different psychoses or different types of dementia have suggested that many of these conditions result from diminished function of neurons that secrete a specific neurotransmitter. Use of appropriate drugs to counteract loss of the respective neurotransmitter has been successful in treating some patients.

In Chapter 56, we discussed the cause of Parkinson's disease. This disease results from loss of neurons in the substantia nigra whose nerve endings secrete *dopamine* in the caudate nucleus and putamen. Also in Chapter 56, we pointed out that in Huntington's disease, loss of GABA-secreting neurons and acetylcholine-secreting neurons is associated with *specific abnormal motor patterns* plus *dementia* occurring in the same patient.

### Depression and Manic-Depressive Psychoses—Decreased Activity of the Norepinephrine and Serotonin Neurotransmitter Systems

Much evidence has accumulated suggesting that *mental depression psychosis*, which occurs in about 8 million people

in the United States, might be caused by *diminished formation in the brain of norepinephrine or serotonin, or both.* (New evidence has implicated still other neurotransmitters.) Depressed patients experience symptoms of grief, unhappiness, despair, and misery. In addition, they often lose their appetite and sex drive and have severe insomnia. Often associated with these is a state of psychomotor agitation despite the depression.

Moderate numbers of *norepinephrine-secreting neurons* are located in the brain stem, especially in the *locus ceruleus.* These neurons send fibers upward to most parts of the brain limbic system, thalamus, and cerebral cortex. Also, many *serotonin-producing neurons* located in the *midline raphe nuclei* of the lower pons and medulla send fibers to many areas of the limbic system and to some other areas of the brain.

A principal reason for believing that depression might be caused by diminished activity of norepinephrine- and serotonin-secreting neurons is that drugs that block secretion of norepinephrine and serotonin, such as reserpine, frequently cause depression. Conversely, about 70 percent of depressive patients can be treated effectively with drugs that increase the excitatory effects of norepinephrine and serotonin at the nerve endings—for instance, (1) *monoamine oxidase inhibitors,* which block destruction of norepinephrine and serotonin once they are formed, and (2) *tricyclic antidepressants,* such as *imipramine* and *amitriptyline,* which block reuptake of norepinephrine and serotonin by nerve endings so that these transmitters remain active for longer periods after secretion.

Mental depression can be treated by electroconvulsive therapy—commonly called "shock therapy." In this therapy, electrical current is passed through the brain to cause a generalized seizure similar to that of an epileptic attack. This has been shown to enhance norepinephrine activity.

Some patients with mental depression alternate between depression and mania, which is called either *bipolar disorder* or *manic-depressive psychosis,* and fewer patients exhibit only mania without the depressive episodes. Drugs that diminish the formation or action of norepinephrine and serotonin, such as lithium compounds, can be effective in treating the manic phase of the condition.

It is presumed that the norepinephrine and serotonin systems normally provide drive to the limbic areas of the brain to increase a person's sense of well-being, to create happiness, contentment, good appetite, appropriate sex drive, and psychomotor balance—although too much of a good thing can cause mania. In support of this concept is the fact that pleasure and reward centers of the hypothalamus and surrounding areas receive large numbers of nerve endings from the norepinephrine and serotonin systems.

## Schizophrenia—Possible Exaggerated Function of Part of the Dopamine System

Schizophrenia comes in many varieties. One of the most common types is seen in the person who hears voices and has delusions of grandeur, intense fear, or other types of feelings that are unreal. Many schizophrenics are highly paranoid, with a sense of persecution from outside sources. They may develop incoherent speech, dissociation of ideas, and abnormal sequences of thought, and they are often withdrawn, sometimes with abnormal posture and even rigidity.

There are reasons to believe that schizophrenia results from one or more of three possibilities: (1) multiple areas in the cerebral cortex *prefrontal lobes* in which neural signals have become blocked or where processing of the signals becomes dysfunctional because many synapses normally excited by the neurotransmitter *glutamate* lose their responsiveness to this transmitter; (2) excessive excitement of a group of neurons that secrete *dopamine* in the behavioral centers of the brain, including in the frontal lobes; and/or (3) abnormal function of a crucial part of the brain's *limbic behavioral control system centered around the hippocampus.*

The reason for believing that the prefrontal lobes are involved in schizophrenia is that a schizophrenic-like pattern of mental activity can be induced in monkeys by making multiple minute lesions in widespread areas of the prefrontal lobes.

Dopamine has been implicated as a possible cause of schizophrenia because many patients with Parkinson's disease develop schizophrenic-like symptoms when they are treated with the drug called L-dopa. This drug releases dopamine in the brain, which is advantageous for treating Parkinson's disease, but at the same time it depresses various portions of the prefrontal lobes and other related areas.

It has been suggested that in schizophrenia excess dopamine is secreted by a group of dopamine-secreting neurons whose cell bodies lie in the ventral tegmentum of the mesencephalon, medial and superior to the substantia nigra. These neurons give rise to the so-called *mesolimbic dopaminergic system* that projects nerve fibers and dopamine secretion into the medial and anterior portions of the limbic system, especially into the hippocampus, amygdala, anterior caudate nucleus, and portions of the prefrontal lobes. All of these are powerful behavioral control centers.

An even more compelling reason for believing that schizophrenia might be caused by excess production of dopamine is that many drugs that are effective in treating schizophrenia—such as chlorpromazine, haloperidol, and thiothixene—all either decrease secretion of dopamine at dopaminergic nerve endings or decrease the effect of dopamine on subsequent neurons.

Finally, possible involvement of the hippocampus in schizophrenia was discovered recently when it was learned that *in schizophrenia, the hippocampus is often reduced in size,* especially in the dominant hemisphere.

### Alzheimer's Disease—Amyloid Plaques and Depressed Memory

Alzheimer's disease is defined as premature aging of the brain, usually beginning in midadult life and progressing rapidly to extreme loss of mental powers—similar to that seen in very, very old age. The clinical features of Alzheimer's disease include (1) an amnesic type of memory impairment, (2) deterioration of language, and (3) visuospatial deficits. Motor and sensory abnormalities, gait disturbances, and seizures are uncommon until the late phases of the disease. One consistent finding in Alzheimer's disease is loss of neurons in that part of the limbic pathway that drives the memory process. Loss of this memory function is devastating.