

## CHAPTER 1

# PSYCHOSIS AND SCHIZOPHRENIA

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*Psychosis* is a difficult term to define and is frequently misused, not only in the newspapers and movies and on television, but unfortunately among mental health professionals as well. Stigma and fear surround the concept of psychosis and the

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Table 1–1. *Disorders in which psychosis is a defining feature*

Schizophrenia
Substance-induced (i.e., drug-induced) psychotic disorders
Schizophreniform disorder
Schizoaffective disorder
Delusional disorder
Brief psychotic disorder
Shared psychotic disorder
Psychotic disorder due to a general medical condition

average citizen worries about long-standing myths of “mental illness,” including “psychotic killers,” “psychotic rage,” and the equivalence of “psychotic” with the pejorative term “crazy.”

There is perhaps no area of psychiatry where misconceptions are greater than in the area of psychotic illnesses. The reader is well served to develop an expertise on the facts about the diagnosis and treatment of psychotic illnesses in order to dispel unwarranted beliefs and to help destigmatize this devastating group of illnesses. This chapter is not intended to list the diagnostic criteria for all the different mental disorders in which psychosis is either a defining feature or an associated feature. The reader is referred to standard reference sources (DSM-IV and ICD-10) for that information. Although schizophrenia will be emphasized here, we will approach psychosis as a syndrome associated with a variety of illnesses which are all targets for antipsychotic drug treatment.

### Clinical Description of Psychosis

Psychosis is a syndrome, which is a mixture of symptoms that can be associated with many different psychiatric disorders but is not a specific disorder itself in diagnostic schemes such as DSM-IV or ICD-10. At a minimum, psychosis means delusions and hallucinations. It generally also includes symptoms such as disorganized speech, disorganized behavior, and gross distortions of reality testing.

Therefore, psychosis can be considered to be a set of symptoms in which a person’s mental capacity, affective response, and capacity to recognize reality, communicate, and relate to others are impaired. Psychotic disorders have psychotic symptoms as their defining features, but there are other disorders in which psychotic symptoms may be present but are not necessary for the diagnosis.

Those *disorders that require the presence of psychosis* (Table 1–1) as a *defining* feature of the diagnosis include schizophrenia, substance-induced (i.e., drug-induced) psychotic disorder, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, and psychotic disorder due to a general medical condition. *Disorders that may or may not have psychotic symptoms* (Table 1–2) as an *associated* feature include mania and depression as well as several cognitive disorders such as Alzheimer’s dementia.

Psychosis itself can be paranoid, disorganized-excited, or depressive. Perceptual distortions and motor disturbances can be associated with any type of psychosis.

Table 1–2. *Disorders in which psychosis is an associated feature*

Mania
Depression
Cognitive disorders
Alzheimer dementia

*Perceptual distortions* include being distressed by hallucinatory voices; hearing voices that accuse, blame, or threaten punishment; seeing visions; reporting hallucinations of touch, taste, or odor; or reporting that familiar things and people seem changed. *Motor disturbances* are peculiar, rigid postures; overt signs of tension; inappropriate grins or giggles; peculiar repetitive gestures; talking, muttering, or mumbling to oneself; or glancing around as if hearing voices.

### ***Paranoid Psychosis***

In paranoid psychosis, the patient has paranoid projections, hostile belligerence, and grandiose expansiveness. *Paranoid projection* includes preoccupation with delusional beliefs; believing that people are talking about oneself; believing one is being persecuted or conspired against; and believing people or external forces control one's actions. *Hostile belligerence* is verbal expression of feelings of hostility; expressing an attitude of disdain; manifesting a hostile, sullen attitude; manifesting irritability and grouchiness; tending to blame others for problems; expressing feelings of resentment; and complaining and finding fault, as well as expressing suspicion of people. *Grandiose expansiveness* is exhibiting an attitude of superiority; hearing voices that praise and extol; and believing one has unusual powers, is a well-known personality, or has a divine mission.

### ***Disorganized-Excited Psychosis***

In a disorganized-excited psychosis, there is conceptual disorganization, disorientation, and excitement. *Conceptual disorganization* can be characterized by giving answers that are irrelevant or incoherent; drifting off the subject; using neologisms; or repeating certain words or phrases. *Disorientation* is not knowing where one is, the season of the year, the calendar year, or one's own age. *Excitement* is expressing feelings without restraint; manifesting hurried speech; exhibiting an elevated mood or an attitude of superiority; dramatizing oneself or one's symptoms; manifesting loud and boisterous speech; exhibiting overactivity or restlessness; and exhibiting excess of speech.

### ***Depressive Psychosis***

Depressive psychosis is characterized by retardation, apathy, and anxious self-punishment and blame. *Retardation and apathy* are manifested by slowed speech; indifference to one's future; fixed facial expression; slowed movements; deficiencies

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in recent memory; blocking in speech; apathy toward oneself or one's problems; slovenly appearance; low or whispered speech; and failure to answer questions. *Anxious self-punishment and blame* involve the tendency to blame or condemn oneself; anxiety about specific matters; apprehensiveness regarding vague future events; an attitude of self-deprecation; manifesting a depressed mood; expressing feelings of guilt and remorse; preoccupation with suicidal thoughts, unwanted ideas, and specific fears; and feeling unworthy or sinful.

This discussion of clusters of psychotic symptoms does not constitute diagnostic criteria for any psychotic disorder. It is given merely as a description of several types of symptoms in psychosis to give the reader an overview of the nature of behavioral disturbances associated with the various psychotic illnesses.

### Five Symptom Dimensions in Schizophrenia

Although schizophrenia is the most common and best known psychotic illness, it is not synonymous with psychosis but is just one of many causes of psychosis. Schizophrenia affects 1% of the population, and in the United States there are over 300,000 acute schizophrenic episodes annually. Between 25 and 50% of schizophrenia patients attempt suicide, and 10% eventually succeed, contributing to a mortality rate eight times as high as that of the general population. In the United States over 20% of all Social Security benefit days are used for the care of schizophrenic patients. The direct and indirect costs of schizophrenia in the United States alone are estimated to be in the tens of billions of dollars every year.

Schizophrenia by definition is a disturbance that must last for six months or longer, including at least one month of delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms. *Delusions* usually involve a misinterpretation of perceptions or experiences. The most common type of delusion in schizophrenia is persecutory, but the delusions may include a variety of other themes, including referential (i.e., erroneously thinking that something refers to oneself), somatic, religious, or grandiose. *Hallucinations* may occur in any sensory modality (e.g., auditory, visual, olfactory, gustatory, and tactile), but auditory hallucinations are by far the most common and characteristic hallucinations in schizophrenia.

Although not recognized formally as part of the diagnostic criteria for schizophrenia, numerous studies subcategorize the symptoms of this illness (as well as symptoms of some other disorders) into five dimensions: positive symptoms, negative symptoms, cognitive symptoms, aggressive/hostile symptoms, and depressive/anxious symptoms (Fig. 1–1). Several illnesses other than schizophrenia share these symptoms dimensions as well (Figs. 1–2 to 1–6).

#### *Positive Symptoms*

Positive symptoms seem to reflect an *excess* of normal functions (Table 1–3) and typically include delusions and hallucinations; they may also include distortions or exaggerations in language and communication (disorganized speech), as well as in behavioral monitoring (grossly disorganized or catatonic or agitated behavior).

Disorders in addition to schizophrenia that can have positive symptoms include bipolar disorder, schizoaffective disorder, psychotic depression, Alzheimer's disease

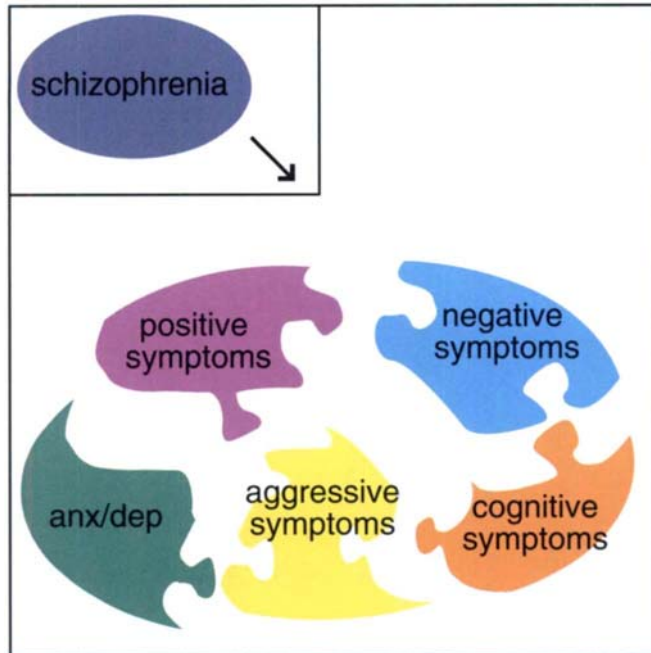


FIGURE 1–1. The **five symptom dimensions** of schizophrenia include not only positive and negative symptoms but also cognitive symptoms, aggressive/hostile symptoms, and depressive and anxious symptoms (anx/dep).

and other organic dementias, childhood psychotic illnesses, drug induced psychoses, and others (Fig. 1–2).

### *Negative Symptoms*

Negative symptoms (Table 1–4) include at least five types of symptoms (all starting with the letter *a*): (1) *affective flattening*, consisting of restrictions in the range and intensity of emotional expression; (2) *alogia*, consisting of restrictions in the fluency and productivity of thought and speech; (3) *avolition*, consisting of restrictions in the initiation of goal-directed behavior; (4) *anhedonia*, that is, lack of pleasure; and (5) *attentional impairment*.

Negative symptoms commonly are considered a *reduction* in normal functions in schizophrenia, such as blunted affect, emotional withdrawal, poor rapport, passivity, and apathetic social withdrawal. Difficulty in abstract thinking, stereotyped thinking, and lack of spontaneity are associated with long periods of hospitalization and poor social functioning.

Negative symptoms in schizophrenia can be either primary or secondary (Fig. 1–3). Primary negative symptoms are considered to be those that are core to primary deficits of schizophrenia itself. Other core deficits of schizophrenia that may manifest themselves as negative symptoms may be those associated with or thought to be secondary to the positive symptoms of psychosis. Other negative symptoms are considered to be secondary to extrapyramidal symptoms (EPS), especially those

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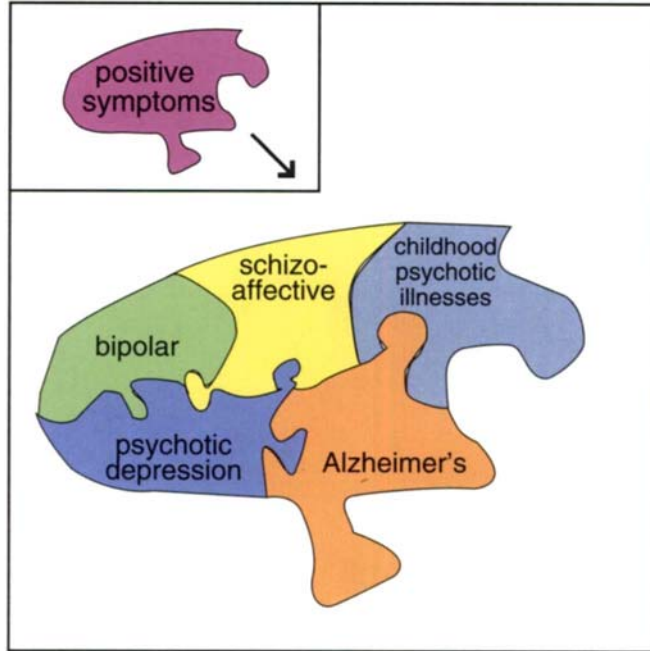


FIGURE 1–2. **Positive symptoms** are associated not just with schizophrenia, but also with bipolar disorder, schizoaffective disorder, childhood psychotic illnesses, psychotic depression, Alzheimer’s disease, and other disorders as well.

caused by antipsychotic drugs. Negative symptoms can also be secondary to depressive symptoms or to environmental deprivation.

### *Cognitive Symptoms*

Cognitive symptoms of schizophrenia and other illnesses of which psychosis may be an associated feature can overlap with negative symptoms. They include specifically the thought disorder of schizophrenia and the sometimes odd use of language, including incoherence, loose associations, and neologisms. Impaired attention and impaired information processing are other specific cognitive impairments associated with schizophrenia. In fact, the most common and the most severe of the cognitive impairments in schizophrenia can include impaired verbal fluency (ability to produce spontaneous speech), problems with serial learning (of a list of items or a sequence of events), and impairment in vigilance for executive functioning (problems with sustaining and focusing attention, concentrating, prioritizing, and modulating behavior based on social cues).

Schizophrenia is certainly not the only disorder with such impairments in cognition. Autism, poststroke dementia, Alzheimer’s disease, and many other organic dementias (parkinsonian/Lewy body dementia, frontotemporal/Pick’s dementia, etc.) are also associated with some cognitive dysfunctions similar to those seen in schizophrenia (Fig. 1–4).

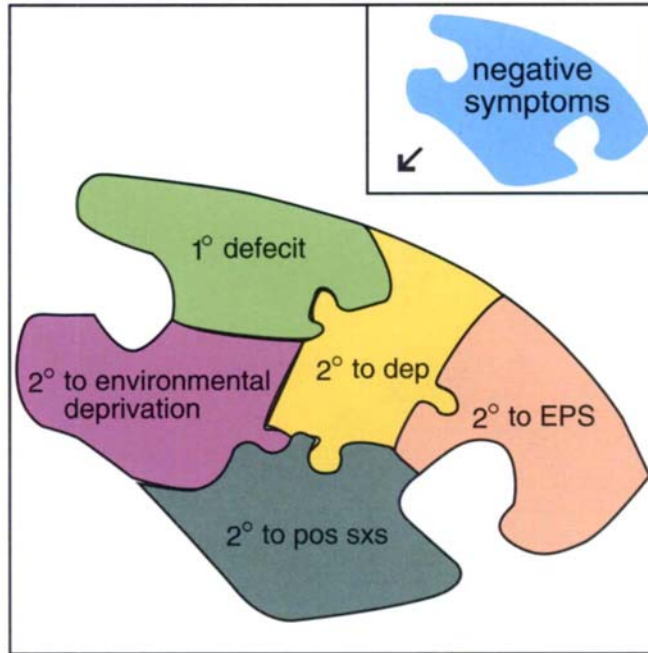


FIGURE 1–3. **Negative symptoms** in schizophrenia can either be a primary deficit of the illness (1° deficit) or secondary to depression (2° to dep), secondary to extrapyramidal symptoms (2° to EPS), secondary to environmental deprivation, or even secondary to positive symptoms (2° to pos sxs) in schizophrenia.

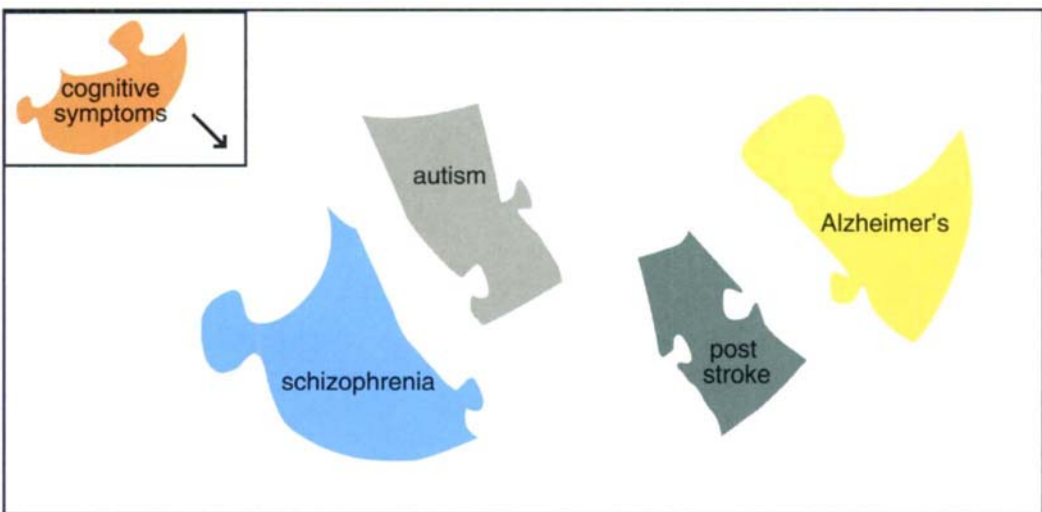


FIGURE 1–4. **Cognitive symptoms** are not just associated with schizophrenia, but also with several other disorders, including autism, Alzheimer's disease, and conditions following cerebrovascular accidents (poststroke).



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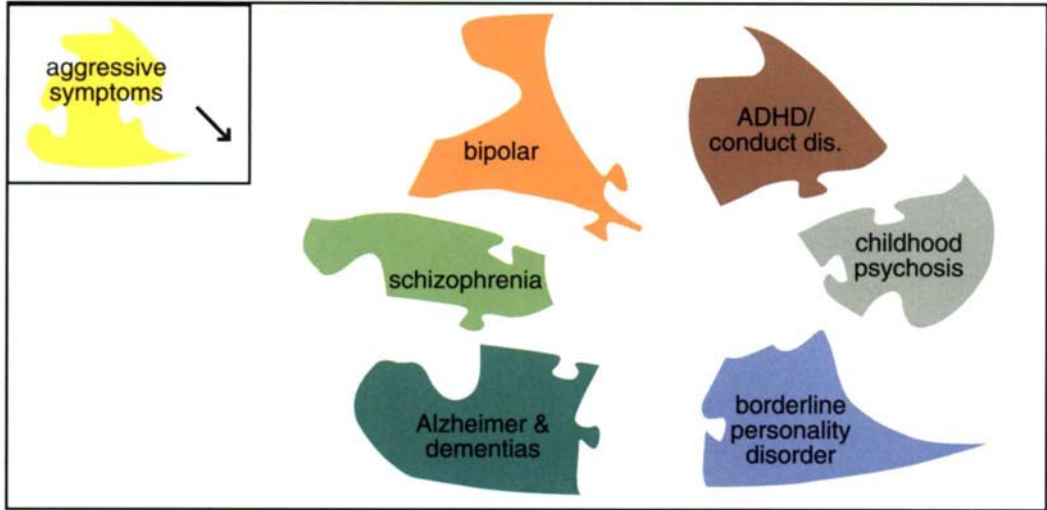


FIGURE 1–5. **Aggressive symptoms and hostility** are associated with several conditions in addition to schizophrenia, including bipolar disorder, attention deficit hyperactivity disorder (ADHD) and conduct disorder (conduct dis.), childhood psychosis, Alzheimer’s and other dementias, and borderline personality disorder, among others.

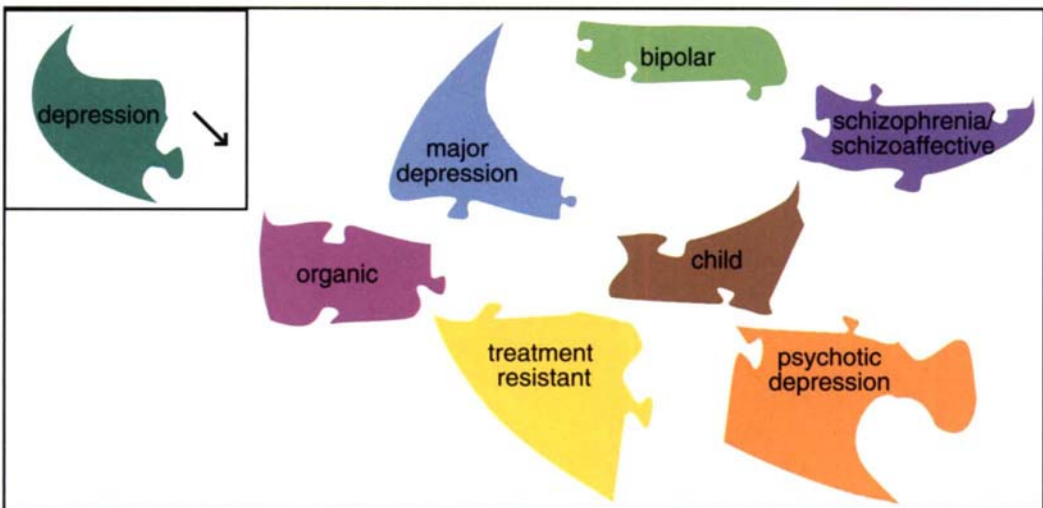


FIGURE 1–6. **Depressive and anxious symptoms** are not only a hallmark of major depressive disorder but are frequently associated with other psychiatric disorders, including bipolar disorder, schizophrenia, and schizoaffective disorder; with organic causes of depression, such as substance abuse; with childhood mood disorders (child); with psychotic forms of depression; and with mood and psychotic disorders resistant to treatment with drugs (treatment-resistant), among others.



Table 1–3. *Positive symptoms of psychosis*

Delusions
Hallucinations
Distortions or exaggerations in language and communication
Disorganized speech
Disorganized behavior
Catatonic behavior
Agitation

Table 1–4. *Negative symptoms of psychosis*

Blunted affect
Emotional withdrawal
Poor rapport
Passivity
Apathetic social withdrawal
Difficulty in abstract thinking
Lack of spontaneity
Stereotyped thinking
Alogia: restrictions in fluency and productivity of thought and speech
Avolition: restrictions in initiation of goal-directed behavior
Anhedonia: lack of pleasure
Attentional impairment

### *Aggressive and Hostile Symptoms*

Aggressive and hostile symptoms can overlap with positive symptoms but specifically emphasize problems in impulse control. They include overt hostility, such as verbal or physical abusiveness or even assault. Such symptoms also include self-injurious behaviors, including suicide and arson or other property damage. Other types of impulsiveness, such as sexual acting out, are also in this category of aggressive and hostile symptoms.

Although aggressive symptoms are common in schizophrenia, they are far from unique to this condition. Thus, these same symptoms are frequently associated with bipolar disorder, childhood psychosis, borderline personality disorder, drug abuse, Alzheimer and other dementias, attention deficit hyperactivity disorder, conduct disorders in children, and many others (Fig. 1–5).

### *Depressive and Anxious Symptoms*

Depressive and anxious symptoms are frequently associated with schizophrenia, but this does not necessarily mean that they fulfill the diagnostic criteria for a comorbid anxiety or affective disorder. Nevertheless, depressed mood, anxious mood, guilt, tension, irritability, and worry frequently accompany schizophrenia. These various symptoms are also prominent features of major depressive disorder, psychotic depression, bipolar disorder, schizoaffective disorder, organic dementias, and childhood

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psychotic disorders, among others, and particularly of treatment-resistant cases of depression, bipolar disorder, and schizophrenia (Fig. 1–6).

**Four Key Dopamine Pathways and the Biological Basis of Schizophrenia**

The biological basis of schizophrenia remains unknown. However, the monoamine neurotransmitter dopamine has played a key role in hypotheses about certain aspects of the five dimensions of symptoms in schizophrenia, discussed above.

Four well-defined dopamine pathways in the brain are shown in Figure 1–7. They include the mesolimbic dopamine pathway, the mesocortical dopamine pathway, the nigrostriatal dopamine pathway, and the tuberoinfundibular dopamine pathway.

***Mesolimbic Dopamine Pathway and the Dopamine Hypothesis of the Positive Symptoms of Psychosis***

The *mesolimbic dopamine pathway* projects from dopaminergic cell bodies in the ventral tegmental area of the brainstem to axon terminals in limbic areas of the brain, such as the nucleus accumbens (Fig. 1–8). This pathway is thought to have an important role in emotional behaviors, especially auditory hallucinations but also delusions and thought disorder (Fig. 1–9).

For more than 25 years, it has been observed that diseases or drugs that increase dopamine will enhance or produce positive psychotic symptoms, whereas drugs that decrease dopamine will decrease or stop positive symptoms. For example, stimulant drugs such as amphetamine and cocaine release dopamine and if given repetitively, can cause a paranoid psychosis virtually indistinguishable from schizophrenia. Also, all known antipsychotic drugs capable of treating positive psychotic symptoms are blockers of dopamine receptors, particularly D2 dopamine receptors. Antipsychotic drugs are discussed in Chapter 2. These observations have been formulated into a theory of psychosis sometimes referred to as the dopamine hypothesis of schizophrenia. Perhaps a more precise modern designation is the *mesolimbic dopamine hypothesis of positive psychotic symptoms*, since it is believed that it is hyperactivity specifically in this particular dopamine pathway that mediates the positive symptoms of psychosis (Fig. 1–9). Hyperactivity of the mesolimbic dopamine pathway hypothetically accounts for positive psychotic symptoms whether those symptoms are part of the illness of schizophrenia or of drug-induced psychosis, or whether positive psychotic symptoms accompany mania, depression, or dementia. Hyperactivity of mesolimbic dopamine neurons may also play a role in aggressive and hostile symptoms in schizophrenia and related illnesses, especially if serotonergic control of dopamine is aberrant in patients who lack impulse control.

***Mesocortical Dopamine Pathway***

A pathway related to the mesolimbic dopamine pathway is the *mesocortical dopamine pathway* (Fig. 1–10). Its cell bodies arise in the ventral tegmental area of the brainstem, near the cell bodies for the dopamine neurons of the mesolimbic dopamine pathway. However, the mesocortical dopamine pathway projects to areas of the cerebral cortex, especially the limbic cortex. The role of the mesocortical dopamine