Hallucinations and delusions—two diagnostic features of psychosis shared across the spectrum of heterogeneous schizophrenia constructs—can be described in terms of the pathophysiology of sensory information processing: hallucination is the impaired ability to classify representations as internally or externally generated, while delusion is the immutable linking of representations with each other in the absence of external dependency. The key anatomical systems in higher-order information processing are the cortex, thalamus, basal ganglia, and medial temporal lobe, each of which is modulated by neurotransmitter projection systems. Preliminary evidence, concentrating to date on the dorsolateral prefrontal cortex, thalamus, and hippocampal region of the medial temporal lobe, points to neural circuitry dysfunction within and between each system in psychosis. This may account for specific symptoms and associated cognitive deficits such as memory impairment, attention deficit, and language disturbance.

The psychiatric diagnoses dementia praecox (Kraepelin) and group of schizophrenias (Bleuler) were introduced to designate a group of psychiatric patients with similar clinical features, disease course, and outcome. The diagnostic criteria used to define schizophrenia have varied over the last 100 years. They have included several forms of hallucinations and delusions, abnormalities of speech and motor activity, cognitive deficits such as poor attention and impaired memory, and affective disturbance. Schizophrenia is now diagnosed in about 1% of the population worldwide. In the 4th edition of his psychiatry textbook, published in 1893, Kraepelin proposed that three groups of patients, diagnosed with catatonia (Kahlbaum), hebephrenia (Hecker), and dementia paranoides, represent different phenotypes of the same illness which he labeled dementia praecox. We are still struggling to answer the two questions Kraepelin faced 100 years ago: How is schizophrenia different from other psychotic conditions? Is schizophrenia one illness or does it represent different diseases?

The heterogeneity of the schizophrenia construct poses a major hurdle for the study of disease mechanisms and etiology. If the diagnosis covers a broad spectrum of patients who might not share the same symptoms, then the search for one etiology and pathogenesis that could predict treatment response and outcome may be futile. Therefore, schizophrenia researchers have attempted to reduce the complexity of schizophrenia by defining subtypes or dividing schizophrenia into one or more entities. Emil Kraepelin subdivided dementia praecox into subtypes based on the presence of one or more symptoms. His last attempt at subdividing dementia praecox/schizophrenia produced 10 different “clinical forms.” The Diagnostic and Statistical Manual of Mental Disorders (DSM) has followed his tradition and the current version (DSM-IV) recognizes three of his subtypes (paranoid type, disorganized [ie, hebephrenic] type, and cata-
tonic type) and supplements them with two new ones (undifferentiated type and residual type). The Kraepelinian subtypes are defined by the presence, severity, and duration of symptoms, but their validity has been questioned. For example, all subtypes, except the para-noid type, show poor temporal stability and might not represent a trait characteristic. Bleuler acknowledged the heterogeneity of the schizophrenia construct without providing a solution to this puzzle:

I call dementia praecox “schizophrenia” ... I use the word in the singular although it is apparent that the group includes several diseases ... so far we have been unable to discover any natural lines of division within the described clinical picture ... the subdivision of the group of schizophrenias is a task for the future.

A different approach to the complexity of schizophrenia can be traced back to the writings of John Russell Reynolds (1828-1896) and John Hughlings Jackson (1835-1911). Jackson proposed a model of abnormal brain function in neurological and psychiatric disorders based on the evolutionary theory that the brain had developed to increasingly more complex levels. He suggested that higher levels of brain function (eg, cortex) control the function of lower levels (eg, subcortical structures, brain stem). Negative symptoms arise from the paralysis of a given hypothetical level of brain function. Positive symptoms arise when higher levels of brain function are impaired and, due to a lack of inhibition, lower levels become apparent, creating “symptoms” normally not observed. In Jackson’s view, “where there is a positive symptom, a negative symptom must be.”

The positive/negative dichotomy resonated in the community of schizophrenia researchers. It seemed reasonable to divide the signs and symptoms of schizophrenia into those that are characterized by the production of abnormal behavior (positive symptoms) and those that represent a deficiency of normal behavior (negative symptoms) (Table I). It was thought that the two symptom dimensions could differentiate subtypes of schizophrenia. More recently, statistical methods have been applied to study the clustering of signs and symptoms in schizophrenia. If some features occur together with other symptoms more than is likely than by chance alone, then they might share etiology and/or disease mechanisms. Such studies have revealed two-, three-, four-, and five-factor models.

Once subtypes of schizophrenia had been defined, researchers attempted to localize the clinical features to distinct brain regions or neural networks. Southard published one of the first such models in the 1910s and proposed that temporal lesions (especially left superior temporal gyrus hypoplasia) are associated with auditory hallucinations, parietal atrophy and sclerosis are associated with catatonia, and frontal lobe aplasia or atrophy is associated with delusions.

More recently, the positive and negative symptoms were associated with dysfunction of separate neural networks. For example, the positive symptoms of schizo-

| Positive            | Negative            |
|---------------------|---------------------|
| Hallucinations      | Alogia              |
| Delusions           | Affective blunting  |
| Formal thought disorder (language) | Avolition         |
| Bizarre behavior    | Anhedonia           |
|                     | Attentional impairment |

Table I. Signs and symptoms of schizophrenia.
Phrenia have been correlated with temporal lobe abnormalities such as volume reduction and increased blood flow. Conversely, negative symptoms have been associated with decreased prefrontal blood flow. Carpenter and colleagues have suggested that patients with schizophrenia can be classified as deficit syndrome patients (with enduring negative symptoms that are not due to medication and/or depression) and nondeficit patients. They have proposed that deficit patients show more frontal lobe deficits than nondeficit patients, but that both subgroups show temporal lobe abnormalities. So far, studies have reported differential impairment of cognitive function, brain structure, and brain function in deficit and nondeficit schizophrenia. Localizing the signs and symptoms of schizophrenia to neural networks relies on neuroscientific models of how behavior is implemented in the brain. Here we will describe a basic outline of brain–behavior relationships. We will then use this framework to review studies of the neural basis of schizophrenia.

The neural basis of psychosis

In order to develop models of how the brain gives rise to psychosis, we need to define psychosis. Despite controversy about the relative weight given to positive and negative symptoms in the diagnosis of schizophrenia, all classification schemes have included two features, hallucinations and delusions. These two symptoms provide the basis for the definition of psychosis as impaired reality testing. The underlying premise in the definition of psychosis is that the brain’s processing of information, derived from the outside world, is perturbed in psychosis. The processing of sensory information involves three steps: the collection of sensory information through perceptual modules, the creation of a representation, and the production of a response. Sensory organs provide information about physical attributes of incoming information. Details of physical attributes (e.g., temperature, sound frequency, or color) are conveyed through multiple segregated channels within each perceptual module. Integration of the highly segregated sensory information occurs at three levels. The first integration occurs in unimodal association areas, where physical attributes of one sensory domain are linked together. A second level of integration is reached in multimodal association areas, which link physical attributes of different sensory qualities together; and a third level of integration is provided by the interpretation and evaluation of experience. It is at this third level of integration that the brain creates a representation of experience that has the spatiotemporal resolution and full complexity of the outside world. Building on previous theoretical efforts, we propose that the positive psychotic symptoms are due to an imbalance in the generation of representations: (1) the impaired ability to classify representations as internally or externally generated (hallucinations); and (2) the immutable linking of representations with each other in the absence of external dependency (delusions). Following the evaluation and interpretation of the representation, the brain creates a response through a variety of channels, e.g., language, affect, and motor behavior. The diagnosis of psychosis is based on the analysis of these responses. For example, hallucinations, delusions, formal thought disorder, and flat affect are defined by abnormalities of the patient’s language and motor behavior.

Neural circuitry in schizophrenia

Four anatomical systems (i.e., the cortex, the thalamus, the basal ganglia, and the medial temporal lobe) are involved in higher order information processing. The function of these four systems is modulated by several groups of neurons that are characterized by their use of a specific neurotransmitter. First we will provide an overview of how these anatomical systems work together during normal brain function. We will then review, in detail, each of the four systems and how they are perturbed in psychosis.

The thalamus is the gateway to cortical processing for all incoming sensory information, here represented by the three major systems: somatosensory, auditory, and visual. The primary sensory cortex (S1, A1, V1) receives sensory information from the appropriate sensory modules (sensory organ and thalamus). The association cortex integrates information from primary cortices, from subcortical structures, and from brain areas affiliated with memory, to create the representation of experience. The medial temporal lobe serves two major functions in the brain: to integrate multimodal sensory information for storage into and retrieval from memory and to attach limbic valence to sensory information. The basal ganglia are primarily involved in the integration of input from cortical areas, particularly from the motor cortex. They modulate the activity of thalamocortical projections,
thereby creating a cortico-striato-pallido-thalamo-cortical loop.

Four groups of densely packed neurons provide widespread projections to many brain areas: cholinergic neurons in the basal forebrain (BF) and brain stem; dopaminergic neurons in the substantia nigra (SN) and ventral tegmental area (VTA); noradrenergic neurons in the locus ceruleus (LC); and serotonergic neurons in the raphe nuclei (R).

The anatomical organization of the human brain gives rise to several neural circuits, each affiliated with different aspects of brain function. Over the last 100 years of psychosis research, four major hypotheses have been put forward that propose abnormalities of these neural circuits in psychosis. (1) Beginning with Kraepelin, psychosis was thought to be a dysfunction of the association cortex in the frontal lobe, the dorsolateral prefrontal cortex (DLPFC).

(2) Based in part on the observation that temporal lobe seizures often present with hallucinations and delusions, abnormalities of the medial temporal lobe (MTL) were proposed to explain the positive symptoms of psychosis.

(3) The occurrence of psychotic symptoms after the use of amphetamine and cocaine, and the discovery that neuroleptic drugs block dopamine D2 receptors, gave rise to the dopamine hypothesis. (4) More recently, the glutamatergic hypothesis, based in part on the fact that N-methyl-D-aspartate (NMDA) receptor antagonists, such as ketamine and phencyclidine, can cause drug-induced psychotic states, has been put forward.

We will review here the evidence that the four anatomical systems (the cortex, the thalamus, the basal ganglia, and the medial temporal lobe) and their modulation by the neurotransmitter-specific projection systems are abnormal in schizophrenia. Although other brain regions, eg, the cerebellum, have also been implicated in the pathology of schizophrenia, we will not review their role here.

Cortex

The association cortex of the human brain is a six-layered isocortex. Layers 2 and 4 are defined by a high density of small interneurons, ie, neurons that do not send long-ranging projections to other cortical or subcortical areas. In contrast, layers 3 and 5 are defined by a high density of pyramidal cells, which collect input through their dendrites and project to other cortical or subcortical areas. Interneurons are GABAergic cells (GABA: gamma-aminobutyric acid) and exert an inhibitory influence on their targets (via GABA_A receptors) whereas pyramidal cells are glutamatergic and have an excitatory influence. Normal cortical function depends on an intricate balance between GABAergic inhibition and glutamatergic excitation.

Neuronal architecture

The anatomical and functional organization of the association cortex, especially the DLPFC, has been studied extensively in schizophrenia. Volume reduction of the association cortex in schizophrenia has been reported in several postmortem and neuroimaging studies. However, there is no marked loss of neurons or increased gliosis, a marker for the degeneration of neurons. Several subtle, yet significant, changes in the cortical architecture have been reported. First, a small subset of cortical neurons that express the enzyme nicotinamide adenine dinucleotide phosphate-diaphorase (NADPH-d) was found to be decreased in the frontal and temporal cortex and increased in number in the underlying white matter. Similarly, the distribution of the Cajal-Retzius cells was shifted to lower parts of the first cortical layer. Second, increased cell density in the frontal and occipital cortex has been described and attributed to changes in cortical neuropil. Third, several abnormalities of GABAergic interneurons have been described: reduced release and uptake of GABA at synaptic terminals, decreased expression of the GABA-synthesizing enzyme glutamic acid decarboxylase (GAD), altered expression of GABA_A receptors, and a reduction in axon cartridges of GABAergic chandelier neurons, terminating on the initial segment of pyramidal cell axons. Fourth, the dendritic organization of frontal cortical areas has been found to be abnormal. Fifth, the organization of synaptic connections, studied with the growth-associated protein GAP-43, was abnormal in frontal and visual association cortices.

Neurotransmitter systems

Cortical neurons are targets for ascending fibers arising from the underlying white matter. Some of these inputs originate from other cortical areas or from the thalamus. Others arise from neurotransmitter-specific projection systems, such as the dopaminergic neurons of the VTA and the serotonergic neurons of the raphe.
nuclei. Modulation of cortical function, via the D_1, D_4, D_5, and 5-HT_2A receptors, leads to the “fine tuning” of information processing, for example, by increasing the signal-to-noise ratio during corticocortical and thalamocortical neurotransmission.

The effect of DA on cortical neurons is conveyed by three DA receptors, the D_1, D_4, and D_5 receptors. The D_1 and D_5 receptors are expressed primarily, but not exclusively, on pyramidal cells, whereas the D_4 receptor is expressed primarily on GABAergic interneurons.

Compared to typical neuroleptics, which have a high D_2-blocking ability, the atypical neuroleptics are much more effective in blocking D_4 receptors. It is not clear whether some of the antipsychotic effects of atypical neuroleptics are conveyed through the D_4 receptors localized on GABAergic interneurons of the association cortex, especially the DLPFC.

Alterations of the GABAergic system and the D_1 receptors of the DLPFC have been reported in schizophrenia. The expression of cortical D_1 receptors is increased by the chronic treatment with typical neuroleptics. Of interest, a recent positron emission tomography (PET) study found a reduction in cortical D_1 receptors, which was correlated with the severity of negative symptoms and poor performance on the Wisconsin Card Sorting Test.

One serotonergic receptor, the 5-HT_2A subtype, is of relevance for the pathophysiology of psychosis. Hallucinogens, eg, lysergic acid diethylamide (LSD), act as agonists at the 5-HT_2A receptor and several antipsychotic compounds, especially the atypical neuroleptics, block the activity of the 5-HT_2A receptor. Several postmortem studies have reported a decrease in 5-HT_2 receptors in schizophrenia, but others have not. A recent PET study of neuroleptic-free patients with schizophrenia did not find any differences in the expression of cortical 5-HT_2 receptors in several cortical areas.

**Cortical function**

Neuroimaging studies have revealed dysfunctional cortical networks in schizophrenia. Regional cerebral blood flow (rCBF) and glucose metabolism were found to be abnormal in frontal cortex and temporal lobe structures at rest as well as during the performance of cognitive tasks. There is, however, no pattern that is diagnostic for schizophrenia. For example, frontal cortical activity at rest was found to be lower by some investigators but not by others, and temporal lobe activity at rest was found to be decreased, or normal, or increased. Similarly, frontal cortical recruitment during task performance was found to be decreased in some studies but not in others.

The clinical heterogeneity of schizophrenia might explain why schizophrenia as a whole is not associated with a pathognomonic abnormality of brain function. When the signs and symptoms of schizophrenia are used to categorize patients into two groups (positive and negative syndrome) or into distinct clusters, a more consistent pattern of neural dysfunction in schizophrenia emerges. Frontal cortex activity at rest correlates inversely with the degree of negative symptoms, and left medial temporal lobe activity at rest correlates positively with the severity of psychopathology, or the degree of reality distortion. Similarly, decreased frontal cortex recruitment during the performance of some cognitive tasks occurs primarily in patients with negative symptoms.

**Thalamus**

The thalamus serves several important functions in information processing in the human brain. First, the relay nuclei (ventral posterior lateral nucleus [VPL], medial geniculate nucleus [MGN], lateral geniculate nucleus [LGN]) relay sensory information from the sensory organs to the appropriate areas of the primary sensory cortex (S1, A1, and V1). Second, the association nuclei, especially the mediodorsal (MD) nucleus, establish reciprocal connections with the association cortex. Third, the motor nuclei (ventral) relay input from the basal ganglia to the motor and premotor cortex. Two abnormalities of thalamic function have been proposed in schizophrenia. First, a breakdown of the sensory filter could lead to an increased stimulation of primary sensory cortical areas. Such a defective filter would implicate abnormalities in the thalamic relay nuclei. Second, dysfunction of the MD nucleus could lead to impairments of cortical association areas, especially the DLPFC. Direct evidence for an involvement of the thalamus in the pathophysiology of schizophrenia is still limited. The most convincing evidence comes from morphometric studies, pointing to a volume reduction of the thalamus, especially the MD nucleus, which has been attributed to cell loss. A postmortem study reported a decrease in parvalbumin-positive neurons in the anteroventral nucleus, which would result in a loss of thalamocortical
projections to the prefrontal cortex.134 Recently, some135,136 but not all,137,138 neuroimaging studies have revealed smaller thalamic volume. In addition, thalamic metabolism and blood flow were found to be impaired at rest and during the performance of cognitive tasks.139,140 Of interest, the decrease in metabolism during the performance of a serial verbal learning test involved primarily the region of the mediodorsal thalamic nucleus.138

**Basal ganglia**

The basal ganglia include the ventral striatum, the dorsal striatum (caudate and putamen), and the globus pallidus. The dorsal striatum (caudate, putamen) receives input from motor cortex and projects to the globus pallidus. The globus pallidus relays the neostriatal input to the thalamus. The thalamus, in turn, projects back to the cortical areas that gave rise to the corticostriatal projections, thereby closing the cortico-striato-pallido-thalamo-cortical loop. This loop is involved in the generation and control of motor behavior. In contrast, the ventral striatum (the nucleus accumbens) is connected with the amygdala, hippocampus, and hypothalamus, and is therefore considered part of limbic system. Reward and expectancy behavior, and their derailment during drug addiction, involve the recruitment of the nucleus accumbens.

All basal ganglia structures are modulated by neurotransmitter-specific projection systems, in particular by dopaminergic neurons. Dopaminergic neurons of the SN project to the neostriatum (nigrostriatal fibers) and dopaminergic neurons of the VTA project to the nucleus accumbens (mesolimbic fibers) and cortex (mesocortical fibers). The two major DA receptors in the dorsal striatum are the D1 and D2 receptors. The nucleus accumbens expresses primarily the D3 receptor.

The basal ganglia have been a focus of interest in psychosis research for three reasons: as potential sites of neuroleptic drug action at D2 receptors, as a potential site for the generation of abnormal motor behavior during psychosis (eg, catatonia), and as a site for pathology in the limbic system.140-145

**Dopaminergic afferents**

The most extensive search has been at the level of dopamine receptors. Earlier studies reported an increased expression of D2 receptors, but there is now good agreement by most studies that the D2 receptor density is not abnormal in schizophrenia.146 One recent study reported an increased expression of dopamine D3 receptors in the nucleus accumbens.147 In addition to studies of dopamine receptors, there have been recent studies of dopamine release and intrasynaptic dopamine content in the striatum. Two groups have independently reported that the intrasynaptic content of dopamine after treatment with amphetamine is increased in schizophrenia.148-149 Thus, not a tonic increase of dopamine release but an increased phasic release of dopamine could be involved in the pathophysiology of schizophrenia. In addition, the regulation of striatal dopamine activity via afferent fibers originating in the prefrontal cortex is impaired.147

**Striatal structure**

Several structural abnormalities of the basal ganglia in schizophrenia have been reported. First, the volume of basal ganglia structures was reported to be increased in medicated schizophrenic patients.150-154 Striatal volume increase is closely related to the treatment with typical neuroleptics: basal ganglia volume is normal or even decreased in newly diagnosed neuroleptic-naive patients,155 increases over time during treatment with typical neuroleptics, and decreases after patients have been switched to atypical neuroleptics.156-158 The mechanism of this relationship is not clear. Second, recent postmortem studies have provided evidence for an overall increased number of striatal neurons159,160 and for a change in the synaptic organization of the striatum, particularly the caudate nucleus.161 Third, the number of nucleus accumbens neurons was found to be decreased.153

**Medial temporal lobe**

The medial temporal lobe contains the amygdala, the hippocampal region, and superficial cortical areas that cover the hippocampal region and form the parahippocampal gyrus (PHG). The hippocampal region can be subdivided into three subregions: the dentate gyrus (DG), the cornu ammonis (CA) sectors, and the subiculum (Sub). The neurons of the human hippocampal region are arranged in one cellular layer, the pyramidal cell layer. Most pyramidal cell layer neurons are glutamatergic whereas the small contingent of nonpyramidal cells are GABAergic. The serial circuitry of the glutamatergic neurons provide the structural basis for long-
term potentiation, a physiological phenomenon crucial for formation of memory. The PHG receives many projections from multimodal cortical association areas and relays them to the hippocampal region. Intrinsic connections within the hippocampal region allow further processing before the information is referred back to the association cortex. The hippocampus is also closely connected with the limbic system; Papez proposed that the hippocampal formation be recruited via these connections to regulate emotion or to modulate information processing by attaching limbic valence to sensory stimuli.

Hippocampal structure

Many studies have found a subtle (about 5%) hippocampal and parahippocampal volume reduction in schizophrenia. Hippocampal volume reduction does not correlate with the duration of illness or correspond to schizophrenia subtypes such as deficit and nondeficit syndrome. In addition to changes in volume, changes in hippocampal shape have recently been reported. Furthermore, deficits of hippocampal structure (volume, N-acetylaspartate levels) are also found in healthy, first-degree relatives of schizophrenic patients.

Most studies have found no change in the number of hippocampal pyramidal neurons but nonpyramidal cells in the hippocampus (especially in CA2 subregion) seem to be reduced by 40%. Studies of the orientation and position of pyramidal cells within the cornu ammonis subfields and of entorhinal cortex layer 2 cells are inconclusive. There is evidence that the intrinsic hippocampal fiber systems and the reciprocal connections of the hippocampal formation are perturbed, leading to a loss of neuropil and an overall loss of white matter. Synaptic organization is changed, possibly indicating altered plasticity of the hippocampus in schizophrenia. In addition to these postmortem studies, magnetic resonance spectroscopy studies have provided evidence for abnormalities of membrane phospholipids and high-energy phosphate metabolism in the temporal lobe.

Neurotransmitter systems

Glutamate receptors of the kainic acid/AMPA subtype, primarily the GluR1 and GluR2 subunits, are decreased in the hippocampus in schizophrenia. GABA-uptake sites are reduced and GABA receptors are upregulated, possibly due to the loss of GABAAergic hippocampal interneurons. In addition, serotonergic 5-HT1A and 5-HT2 receptors are increased and 5-HT2 uptake sites are unchanged in the hippocampus in schizophrenia.

Hippocampal function

The metabolism and blood flow of the hippocampus are increased at baseline in schizophrenia. Furthermore, hippocampal and parahippocampal rCBF is increased during the experience of psychotic symptoms and correlates with positive symptoms (delusions, hallucinations). Recently, we have shown that hippocampal recruitment during the conscious recollection of semantically encoded words is impaired in schizophrenia. Schizophrenic patients displayed increased levels of hippocampal blood flow at rest and lacked the normal modulation that predicts recall accuracy in control subjects. In addition, there is also indirect evidence for the contribution of hippocampal abnormalities to cognitive impairments seen in schizophrenia.

Hippocampal lesion models of schizophrenia

Additional evidence for a contribution of hippocampal dysfunction to the pathogenesis of schizophrenia is provided by hippocampal lesions in rodents and primates. Hippocampal lesions produce behavioral states that share some resemblance with schizophrenia (attentional and memory deficits, stereotypic behavior, and hyperarousal) and behavioral changes are reversible by neuroleptic drugs. Such lesion models have been established in adult rats, in neonatal rats, and in nonhuman primates.

Conclusion

In summary, the neuropathology of schizophrenia remains elusive. However, postmortem and neuroimaging studies have provided evidence for the
involvement of several neural networks in schizophrenia. Impaired nodes include the dorsolateral prefrontal cortex, the thalamus, and the hippocampal formation. Abnormalities in these structures might explain some of the diagnostic features of schizophrenia as well as the cognitive deficits often seen in schizophrenia, e.g., memory impairment, attentional deficits, and language disturbance. The two leading pharmacological models of schizophrenia, the dopamine and the glutamate model, and their implications for the study of pharmacological responses in schizophrenia, will be discussed in another article in this issue.

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**Basic research**

**Modelos neurales de la esquizofrenia**

Las alucinaciones y los delirios –dos características diagnósticas de las psicosis presentes a través del espectro de los heterogéneos constructos de esquizofrenia– pueden ser descritos en términos de los procesos de información sensorial: la alucinación es el deterioro en la capacidad de clasificar representaciones generadas interna o externamente; en cambio, el delirio es la unión inmutable de representaciones con otras en ausencia de una dependencia externa. Los sistemas anatómicos clave en los procesos de información de orden superior son el córtex, el tálamo, los ganglios basales y el lóbulo temporal medial, cada uno de los cuales es modulado por sistemas de proyección de neurotransmisores. Existen evidencias preliminares que se concentran, a la fecha, en la corteza prefrontal dorsolateral, el tálamo y la región del hipocampo del lóbulo temporal medial y apuntan a disfunciones de los circuitos neurales dentro y entre cada sistema en la psicosis. Esto puede dar cuenta de síntomas específicos y déficit cognitivos asociados como deterioro de la memoria, déficit de la atención y trastornos del lenguaje.

**Modèles neurologiques de la schizophrénie**

Les idées délirantes et les hallucinations – deux symptômes de la schizophrénie, présents dans toutes les formes hétérogènes de cette maladie – peuvent être analysées sur le plan physiopathologique comme un dysfonctionnement du traitement des informations sensorielles : l’hallucination est l’incapacité de définir si une représentation est d’origine intérieure (mentale) ou d’origine externe et les idées délirantes sont dues à l’établissement par le sujet d’une relation immuable entre des représentations qui n’est pas justifiée par les éléments extérieurs. Les structures anatomiques essentielles impliquées dans les processus intellectuels sont le cortex, le thalamus, les ganglions de la base et le lobe temporal médian, chacune étant modulée par des systèmes de projections neuronales utilisant des neurotransmetteurs spécifiques. Les données que nous avions réunies antérieurement, impliquant jusqu’à présent le cortex dorsolateral préfrontal, le thalamus et la région hippocampale du lobe temporal moyen, soulignaient l’existence d’une dysfonction des circuits neuronaux au sein de ces structures et entre elles dans les psychoses. Ces anomalies pourraient expliquer les symptômes spécifiques et les déficits cognitifs associés tels que les troubles de la mémoire, les troubles de l’attention et les troubles du langage.

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