

NEUROBIOLOGICAL SUBSTRATES OF THOUGHT AND PERCEPTION

“If it should be confirmed that the disease attacks by preference the frontal areas of the brain, the central convolutions and the temporal lobes, this distribution would in a certain measure agree with our present views about the site of the psychic mechanisms which are principally injured by the disease.”

E. Kraepelin, *Dementia Praecox*, 1919

(on discussing the anatomical basis of what later became known as schizophrenia)

Performing even routine speech, visual, and motor tasks like carrying on a conversation, following a map to a new classroom, and reading these lecture notes is extraordinarily complex. These tasks become even more complex when environmental demands change. To successfully complete these tasks, a person must selectively attend to specific sensory information, recall relevant stored sensory information, compare the stored information with new information, consider a variety of behavioral responses, select a response, perform that behavior, evaluate its effectiveness, and select an alternative response if the first behavior was ineffective. At the same time, irrelevant thoughts, perceptions and behavioral responses need to be inhibited. Disturbances in one or more of these steps can lead to marked disability. For example, a hallucinating person may recall auditory memories of voices even when sitting in a silent room, or may have considerable difficulty in attending selectively to a conversation due to intrusion of these abnormal perceptions. A person who has impaired ability to evaluate the effectiveness of her speech in communicating meaning may ramble in an incoherent and illogical manner. This can lead to marked social, occupational, and other disabilities. Research indicates that critical brain structures are involved in regulating these aspects of thought and perception. These brain structures include the **prefrontal cortex, cortical and subcortical temporal lobe**, and the related VTA-mesocorticolimbic system discussed earlier. This section examines the role these brain structures and systems play in thought and perceptual processes.

The prefrontal cortex

The **prefrontal cortex** (PFC) lies rostral or in front of the supplementary motor cortex (area 6; Fig. 1). The PFC on the lateral wall of the hemispheres is called the dorsolateral PFC, while that on the ventral surface (over the orbits) and the medial wall is called the ventromedial or orbitomedial PFC. The PFC has major afferent and efferent association fiber connections to parietal, occipital, and temporal association cortex, hippocampus, hypothalamus, thalamus, and limbic structures. The PFC has additional major reciprocal connections with auditory association cortex in the temporal region and with visual association cortex (not shown in lower left of Fig 1). Thus, the PFC is ideally situated to **prioritize and integrate sensory input** from one or more of these sensory

modalities into complex perceptions, and to serve as a comparison site for new and old complex perceptions. It also receives afferents from the mediodorsal thalamus. As discussed in the Emotion section, limbic structures act to assign emotional significance to perceptions and to govern the expression of emotions. These connections permit the **PFC to regulate selective attention to the emotional significance of sensory inputs, and to control emotional reactions to changing internal and external sensory inputs.**

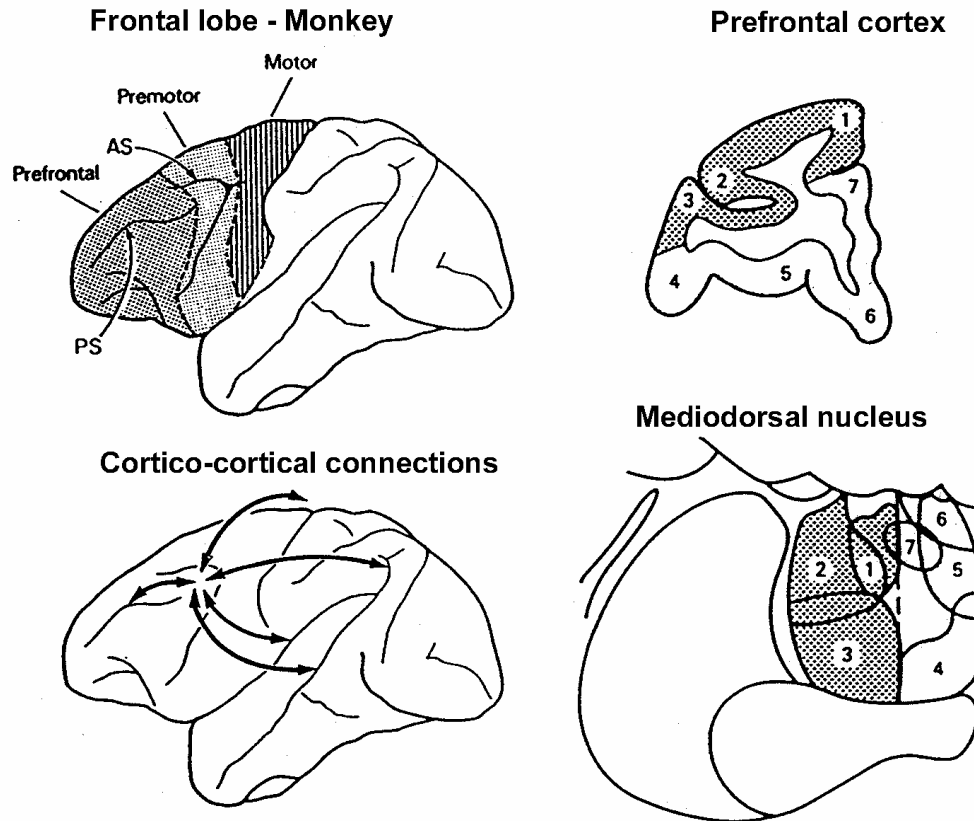


Fig. 1. Schematic drawings of the lateral surface of the human brain showing the prefrontal association cortex in relation to other major cortical regions. The MD projects extensively to the PFC in a topographic manner –see associated numbers in MD and PFC.

The prefrontal cortex is a site critical to short term or “working memory”

The prefrontal cortex is a layer of tissue that lies just behind the forehead. With neural connections to almost all the areas of the brain that process sensory information, it is well situated to maintain a flexible store of information relevant to any task at hand. It is also the part of the brain that has grown the most in humans, as compared with monkeys.

When localized electrical stimulation is applied to the PFC of conscious humans, **no** specific subjective, behavioral, or physiological changes occur (in contrast to stimulation of the amygdala, hypothalamus or temporal cortex). Thus, specific memories are not likely to be **stored** in the PFC. Rather than encoding memories, the PFC, and especially the dorsolateral PFC, appears to integrate processing and recall of specific perceptions and responses that are stored in other regions of the brain. A major role of the PFC is to permit **working memory**, which is the limited, short-term store of currently relevant information that we draw on when we comprehend a sentence, follow a previously decided plan of action or remember a telephone number. When we bring to mind the name of the medical school Dean, for instance, that information is temporarily copied from long-term memory into working memory, which combines moment-to-moment awareness and rapid retrieval of archived information. It has been called the **“blackboard of the mind”** and is used to perform a number of tasks including mental arithmetic, planning a chess move, constructing a sentence, answering an open-ended question, finding a new route home when your usual street route is disrupted by road construction etc.

Evidence implicating the **PFC** in **working memory** comes from studies of human and nonhuman primates. In a classic experiment involving a **delayed response task** (Fig. 2), a monkey briefly views a food morsel located in one of two randomly varied locations. The monkey is allowed to retrieve the food only after a delay in which a screen is lowered, removing the food from sight. This forces the monkey to retain a memory (keep on the mind’s “blackboard”) of the location of the object during the delay period. **Infant** humans, **infant** monkeys, and monkeys with **prefrontal damage** perform poorly on this task, though they are unimpaired in reaching for food when there is no delay. Rather, they reach repeatedly into the box located on the side where food reinforcement was last received. Such repetition is a form of **perseveration** (repetition of a previous response when it is no longer appropriate). Thus, it is not surprising that, after myelination of PFC connections to other association areas at about 8 months, humans display unimpaired, non-perseverative performance on working memory tasks.

Blockade of dopaminergic inputs to the PFC **impairs** performance on working memory tasks in primates. It is helpful to think of everyday examples of working memory as keeping in mind an on-line program of instructions directing your behavior and constantly updating itself when, for example, driving to a friend’s house, going to a class, even going from one room to another. How many of us have arrived at a room and “forgot” why we came there? Or put the cereal box in the refrigerator? This is failure of working memory, and it is likely that some of your prefrontal neurons failed to fire appropriately!

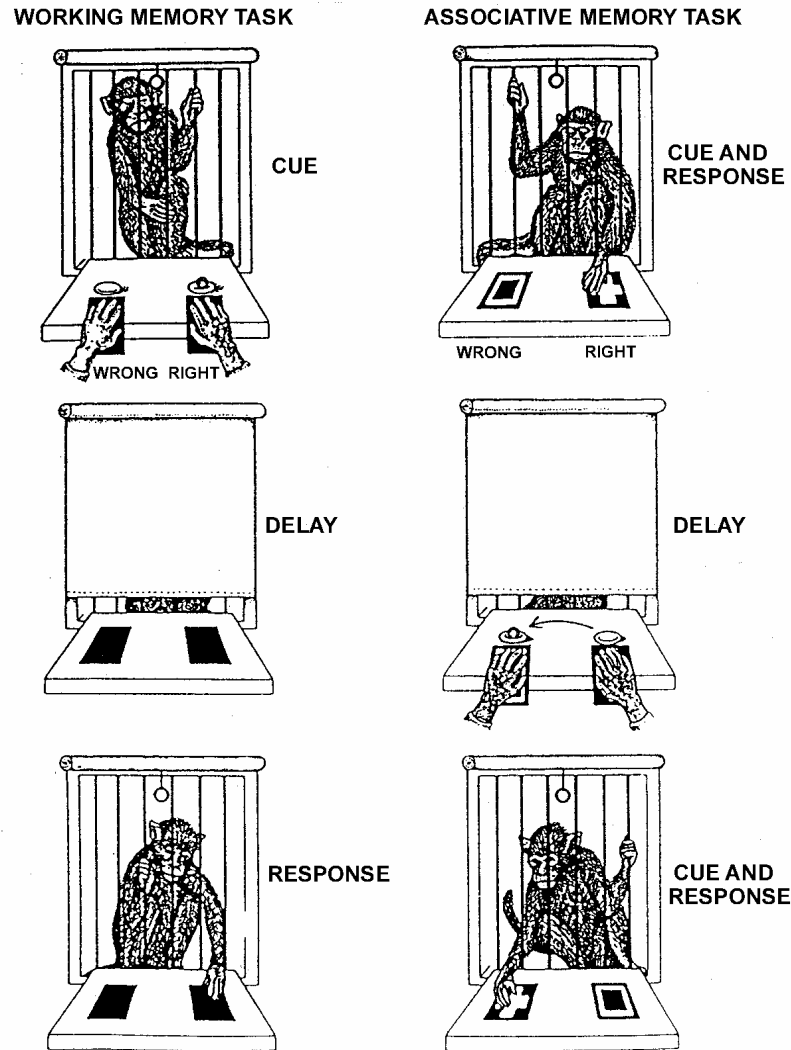


Fig. 2. In the working memory task, the left monkey must "keep in mind" where the target stimulus was during the delay.

Effects of damage to the prefrontal cortex

As mentioned earlier, lesions occurring in the adult human or primate dorsal and lateral PFC impair working memory as indicated by perseverative responses (repetition of a previous response when it is no longer appropriate) on tests in which sorting of objects is required. For example, the **Wisconsin Card Sort Test** requires a person to sort cards displaying various numbers of colored shapes into piles according to the **shape**, **color**, or **number** of objects on a card. The goal is to figure out the **sorting rule**. After each card is placed on one of three piles, the examiner indicates if the card was correctly placed, without revealing the sorting rule (e.g., object shape) chosen. Most people can discern the sorting rule after a few trial-and-error attempts, and then sort successive cards without errors. However, if the examiner then suddenly and secretly **changes** the sorting rule (e.g., object color), a few new trial-and-error attempts are needed before successive card sortings occur. Successful

performance during this task is associated with increased metabolic neuronal activity in the **dorsolateral PFC**, as measured by PET scans. Patients with PFC damage **persist** in previously successful solutions, and fail to alter their choices, even when informed that their sorting choices are no longer correct. This reflects deficient **working memory** (can't keep things on the "blackboard of your mind"). Many patients with **schizophrenia** demonstrate decreased blood flow in the dorsolateral PFC during this task, and have higher rates of perseverative sorting responses. This may explain the finding that many schizophrenics can perform routine tasks without difficulty yet have considerable difficulty following **new** or **complicated** verbal or written instructions. It may also explain why patients with schizophrenia and other CNS disorders (such as dementia) speak in disjointed and illogical sentences (can't keep earlier parts of the sentence or paragraph on their mind's "blackboard" or "scratch pad"), fail to notice their poor hygiene, and engage in **repetitive** behaviors.

Extensive PFC damage or damage localized to the **orbital** (underneath part over the orbits) and **medial** aspects of the **PFC** results in **little** or no loss of **intellectual function**, but in a characteristic **affective and behavioral dyscontrol syndrome**. Individuals with this syndrome display little apparent emotional reactivity to stimuli, appearing **bland**. They often cry, laugh, become angry, or act silly following minor stimulation. They often show inattention toward, or lose interest, in social rules and interpersonal expectations.

Phineas Gage

A famous example involved the case of **Phineas Gage**, a 25-year-old responsible, clever, intelligent, socially well-adapted railroad foreman. Gage was charged with detonations of explosive powder used to break up boulders to permit the laying of railroad tracks. In an accident, Gage sustained **bilateral medial frontal lobotomy** when a tamping rod was propelled through his skull and brain. Gage never lost consciousness, appeared articulate, intelligent, physically fit, and capable of recalling precise details from memory. However, he was profoundly changed in his thought and behavior, and was unable to hold a job. He became "irreverent and capricious," was often profane and inattentive to social conventions, "failed to honor his commitments," and showed little insight into why others considered his arguments and discussions rambling, repetitive and inappropriate.

The interconnections between of the orbito- and medial PFC with the thalamus, hypothalamus, and amygdala are occasionally severed by brain trauma or other injuries. Patients with injuries to orbitomedial PFC often display **docile apathy** and **lack of spontaneity**. Indeed, in the early portion of this century, intractable anxiety and explosive aggressive behavior was occasionally surgically treated by severing these efferent fibers in a procedure termed **prefrontal** leukotomy (cutting the white matter of the frontal lobes). The originator of this procedure, Egas Moniz, received the Nobel Prize for his work. Tragically, though prefrontal leukotomy did reduce explosive aggression and anxiety in many patients, controlled studies showed little advantage in most patients, and often resulted in epilepsy. Additionally, the surgery also resulted in **reduced spontaneity** in patients, and raised serious ethical concerns. Psychosurgery is now nearly abandoned as treatment for aggressive behaviors.

The temporal lobe plays an important role in cognitive and perceptual processes

We have seen that the **prefrontal** cortex plays a primary role in complex "executive" functions and goal directed behavior. The temporal lobe is a second major cortical region involved in higher cognitive functions, including information processing, complex sensory perception, memory and emotion. Although the frontal and temporal lobes are discussed separately, it is perhaps more accurate to consider them together as a cortical **system** is connected by dense, reciprocal anatomical connections between them. Fig. 3. shows various views of the human temporal lobe. Note that the temporal lobe actually consists of several structures. The temporal neocortex (on lateral surface) is phylogenetically "new" cortex. In contrast, the archi- and paleocortex (on medial surface) is phylogenetically "old" cortex and includes the amygdala, hippocampus, uncus, and parahippocampal gyrus.

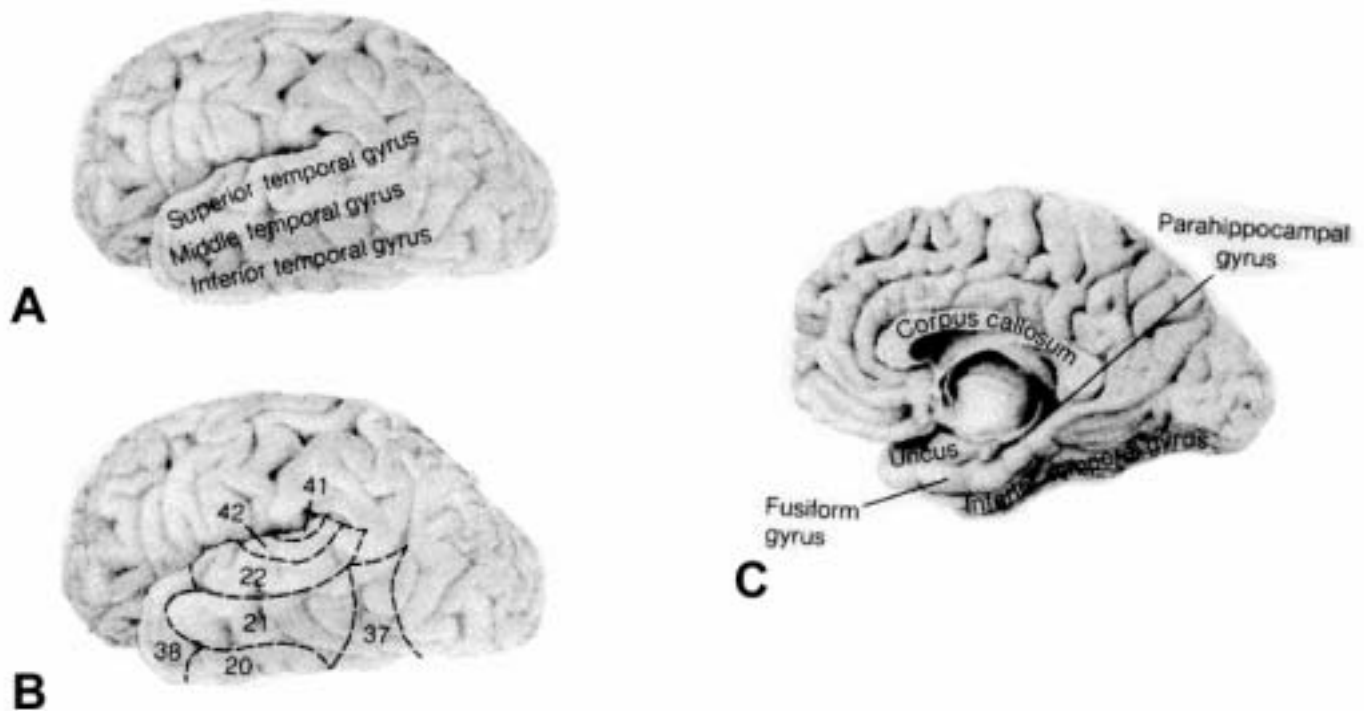


Fig. 3. Gross anatomy of the temporal lobe **A.**, The three major gyri on the lateral surface; **B.**, Brodman's cytoarchitectural zones; **C.**, gyri on the medial surface. The amygdala and hippocampus are embedded deep within the temporal lobe (not shown). (From Kolb and Wishaw, *Human Neuropsychology*, 1985)

The temporal lobe is rich in internal connections, as well as in afferent and efferent connections to other cortical association areas. For example, there are dense reciprocal connections to frontal and parietal association areas. Moreover, there are substantial subcortical projections to the basal ganglia and limbic structures such as hypothalamus and amygdala.

Many **specialized subregions** exist within the temporal lobe. For example, the **amygdala** has a special role in emotion and affect, and the hippocampus has a critical

role in long term memory. The neocortex is also specialized here, consisting of primary and secondary auditory cortex, olfactory and gustatory (taste) cortex, visual association areas and language (Wernicke's; area 22) region. In fact, the temporal lobe, in particular the amygdala and parahippocampal area (feeds into the hippocampus—remember Papez Circuit—hippo-mamm. body-MTT-ant. nuc. thal.-cingulate cortex-cingulum-parahippo.-hippo-hippo) receives a convergence of input from all five sensory modalities.

Temporal lobe damage is associated with certain forms of psychopathology

The complex, multiple functions and areas within the temporal lobe, particularly in the sensory, perceptual and emotional domains, suggest that damage or dysfunction in the temporal lobe would result in disorders of thought, perception, emotion and memory. Indeed, lesions, damage, or surgical removal of temporal lobe structures can result in a wide range of neuropsychological sequelae. The **manifestation** and extent of these disturbances greatly depend on the **extent** and **location** of the damage. Post traumatic damage to the temporal lobes, or destruction following viral diseases such as herpes encephalitis, frequently can present as organic **psychosis** with **delusions**. Similarly, neoplasms and cerebrovascular lesions involving the temporal lobe can induce delusions. For example, in certain rare but remarkable perceptual disturbances (one being **Capgras syndrome**), patients have beliefs that people they know well became "imposters" or "persecutors," or have changed faces. These syndromes are often associated with temporal (and parietal) lobe damage.

Temporal lobe **epilepsy** (TLE), in which the epileptic focus is in the temporal lobe, is often associated with perceptual distortions and disturbed thought patterns. Sufferers of TLE do **not** experience major **motor** convulsions typical of a grand mal seizure, but instead have brief periods of an **altered** mental state, which they may not remember. Hughlings Jackson first described TLEs in 1879, as the "most elaborate psychical states." Subjective reports of experiences during TLE-associated seizures (or from electrical stimulation during surgery) vary among individuals. Perceptual phenomena are common, such as **olfactory and gustatory hallucinations** (specific, yet indefinable sensations of odor or taste). **Auditory and visual hallucinations, illusions of memory, déjà vu**, or familiarity of the unfamiliar, memory flashbacks, changes in awareness (e.g. "out of body" experiences), or feelings of emotion such as fear (most commonly) or pleasure may all occur.

In the 1940s and 50s, the Canadian neurologist Wilder Penfield conducted extensive, systematic stimulation studies of the temporal lobe in awake humans undergoing surgery to localize or remove the epileptic focus. Temporal lobe stimulation produced "experiential" phenomena that generally related to a patient's **past experience**. These mental phenomena can be elicited by stimulation of temporal lobe structures, but virtually **never** by stimulation of other cortical regions. The most commonly reported phenomena were **visual** and **auditory hallucinations** in the form of illusions (see a face,

a scene, hear a voice or music, experience a past event in vivid detail). Consider the following case:

During stereotaxic depth electrode exploration of the temporal lobe, a 22-yr old epileptic patient has been instructed to let us know if he felt something when told that the stimulation had been turned on. After many negative stimulations, the patient noted a feeling when the electrode was placed in the amygdala. He found it difficult to describe but found it strange, somewhat scary, and like falling into water. When stimulation was repeated once more but for longer duration (without warning this time), the patient opened his mouth with an astonished look, sat up and said it was the feeling of being at a picnic in Brewer Park in Ottawa. "A kid was coming up to me to push me into the water. I was pushed by somebody stronger than me. I had experienced that same feeling when I had "petit mals" before." He called it a bad feeling. Upon later questioning, he revealed that this had been a real life event when he was about 8 yrs. old.

In some cases, there is also some association of TLE, particularly left-sided lesions, with a schizophrenic-like psychosis. In one study, of 24 patients with an EEG (electroencephalogram) diagnosis of TLE, **one-half met criteria for schizophrenia**; the most common symptoms were paranoid delusions.

Schizophrenia

For many years, there was no evidence to indicate that schizophrenia was associated with morphological changes in the brain (hence the terms "functional" psychosis versus "organic" psychosis). However, there is now clear evidence that schizophrenia is an organic disease. Postmortem examination of the brains of schizophrenic patients indicates subtle morphological and cellular abnormalities in temporal and frontal lobe structures. We have already discussed the problems with working memory associated with lesions of the PFC.

Ventricular enlargement Many schizophrenic patients, including young and never-medicated patients, show abnormal enlargement of the cerebral ventricles. Ventricular enlargement is **not** pathognomonic (characteristic or diagnostic of a specific disease) to schizophrenia, but is suggestive of cortical tissue loss or atrophy. This finding is particularly evident in the temporal horn of lateral ventricle.

Gross volume changes (from MRI volumetric studies) Many studies concur that the **volume of medial temporal lobe structures** is often **reduced** in schizophrenia. Smaller hippocampal, amygdala, and parahippocampal gyrus volumes are consistently reported. Although many alterations are found bilaterally, abnormalities are more commonly found in the **left** hemisphere. Many researchers have commented that the prominent disorganization of thought and language in schizophrenia may be related to left hemisphere changes. More importantly, the severity of psychosis is positively correlated with the reduction in temporal lobe volume.

Cytoarchitectural alterations in limbic temporal structures A number of investigations have revealed abnormalities in the cellular arrangement of certain cortical regions, particularly in **temporal and frontal regions**. For example, in the parahippocampal gyrus, the pattern of cellular arrangement is disrupted in the brains of schizophrenics and cells are located in the wrong layers. A major current theory of the etiology of schizophrenia is that it represents a genetically influenced disturbance of neural migration.

Hallucinations and regional brain activation

Hallucinations have fascinated investigators interested in psychosis and brain dysfunction. They occur in several psychiatric disorders, but most commonly **schizophrenia**. For many years, people hearing voices were thought simply to be "crazy" - and there were no clues about neural correlates of hallucinations. In recent years, sophisticated brain imaging techniques have found **that hallucinations are associated with changes in temporal lobe glucose metabolism**, especially in the **LEFT hemisphere over the auditory area**. Other researchers recently found that in hallucinating patients, auditory evoked potentials (electrical potentials recorded from the auditory cortex—this is **not** the brain stem auditory evoked potential) were **delayed** (increase in latency) during hallucinations, a pattern also found when normal subjects are distracted by non-target sounds. Another study found a strong correlation between the percent reduction in temporal lobe volume and the severity of hallucinations. It is hypothesized that hallucinations are linked to a distorted interplay between auditory association areas or language regions, and temporal limbic structures.

In summary, the temporal lobe integrates an enormous amount of complex sensory information, both externally and internally generated, and interfaces this processing with the brain's central "affect" system. Thus, we can see that abnormal wiring or firing, or a breakdown in the neural organization of temporal areas, could easily result in psychotic symptoms.

Dopaminergic modulation of thought and perception

In addition to the role played by specific anatomical regions, neurotransmitter systems are also critical for normal functioning. In particular, brain dopaminergic systems have been implicated in thought disorders. As discussed previously, dopamine systems originate in the midbrain VTA (ventral tegmental area) and project to the frontal cortex and limbic structures (mesocorticolimbic). DA projections also reach the temporal lobe. In addition to its role in reward and reinforcement, the mesocorticolimbic dopamine pathway is implicated in **psychosis**.

Three major lines of evidence implicate the dopamine system in abnormal thought and perception. First, **dopaminomimetic drugs** (e.g., amphetamine, cocaine, L-Dopa), which functionally increase CNS dopamine levels, **exacerbate pre-existing psychotic symptoms**. Second, administration of **dopaminomimetic drugs** can **induce** psychotic symptoms in normal individuals. Third, all known **antipsychotic medications** work by **blocking dopamine receptors**.

Dopaminomimetic drugs can induce psychosis

L-Dopa

L-dopa is a metabolic precursor of dopamine and functionally increases CNS dopamine levels. It is the primary drug treatment of Parkinson's disease, and temporarily alleviates the debilitating motor symptoms of this disease due to marked degeneration of the dopaminergic neurons. A relatively common side-effect of high-dose L-dopa therapy is behavioral disturbance due to psychotic symptoms.

Amphetamine and cocaine

As you now know, amphetamine and cocaine produce their psychological effects primarily by inducing massive increases in levels of synaptic dopamine. Occasional use of moderate doses of these compounds usually does not cause psychotic symptoms. However, with chronic high doses a psychotic state can ensue. In the 60's, amphetamine addicts coming into for treatment in the emergency room were often misdiagnosed as schizophrenic. One description of amphetamine psychosis is noted below.

“After ingesting dopaminomimetic drugs, people reported hearing voices commenting on their behavior, threatening them, or telling them to do things. They also reported seeing things that were not there. These hallucinations tend to be intrusive and quite distracting. They would develop delusions, or beliefs that were not true. Some might believe they could fly, others may become convinced that the world would come to an end. Often they would become paranoid, worried, and completely preoccupied with the fear that someone was out to harm them. These symptoms so closely resemble thought disorders such as schizophrenia that people presenting after ingesting amphetamine or cocaine are, at times, diagnosed as schizophrenic.”

One strong possibility is that dopamine release within certain brain regions occurs when you are "attending" to salient events. An over activity of dopamine at these sites may produce **attention abnormalities**, so that stimuli which would normally be ignored are instead considered to be relevant. This is exactly what many schizophrenia researchers believe occurs in schizophrenics. Stimuli that you would normally ignore (for instance background sounds that you are ignoring as you read this discussion, or were ignoring) are not filtered out in schizophrenics. These "irrelevant" events enter consciousness as salient events, and delusional schemes are developed to "explain" the significance of these events

Dopamine-blocking drugs have an antipsychotic effect

Since the discovery of chlorpromazine (Thorazine) in the 1950's, drugs that **block dopamine receptors** (dopamine antagonists) were shown to have a specific **antipsychotic** effect. These drugs, termed **neuroleptics** (“seizing” the brain) or antipsychotics are effective in reducing or eliminating thought disorder, delusions, and hallucinations. Currently, a wide range of antipsychotic medications is available that share a common property of blocking a subtype of dopamine receptor, the D2 receptor. There is a remarkable correlation between the *in vivo* clinical potency of a compound and its affinity for the D2 receptor. The more potent a drug is clinically, the better it binds to these receptors. Binding to many other receptors has been examined, and there is no relationship between binding, for example, to serotonergic, adrenergic, D1, or histaminergic receptors. It is interesting that the D2 receptors lie on striatal neurons that project to the external segment of the GP (indirect pathway) while the D1s lie on striatal cells that project to the internal segment of the GP (direct pathway).

These observations about dopaminomimetic agents and dopamine antagonists suggest clearly that this transmitter is involved in the regulation of normal thought processes. However, there are many unanswered questions about the precise role played by dopamine. Because dopamine fibers innervate structures such as prefrontal cortex, amygdala, septum, and nucleus accumbens, overactivity of dopamine is likely to result in disturbance of neural processing in these limbic regions. This is an appealing hypothesis but as yet unproven. Similarly, the relationship between the antipsychotic effect of neuroleptics and the pathophysiology of schizophrenia is not established.

Problem Solving

1. Which are found in the temporal lobe?
 - A. Broca's area, primary somatosensory cortex, visual association areas
 - B. amygdala, hypothalamus
 - C. Wernicke's area, amygdala, primary auditory cortex
 - D. Broca's and Wernicke's areas, amygdala, hippocampus
 - E. SMA

2. The dopaminergic system functionally links anatomical areas of:
 - A. VTA, dorsal raphe nucleus, and prefrontal cortex
 - B. LC, limbic system, and prefrontal cortex
 - C. VTA, limbic system, and prefrontal cortex
 - D. LC, raphe nucleus, and prefrontal cortex
 - E. dorsal raphe nucleus, basal ganglia, visual cortex

3. Phineas Gage would be likely to:
 - A. forget most past experiences
 - B. not be able to read or write
 - C. forget meeting H.M. or R.B. (pun!)
 - D. make loud jokes in church
 - E. lose his working memory

4. Working memory:
 - A. is stored in the hippocampus
 - B. is damaged following lesions of the dorsolateral PFC
 - C. is used for planning a chess move
 - D. is used for performing mental arithmetic
 - E. three of the above are **TRUE**

5. Which of the following statement is **TRUE** regarding the phrase “purple rounding to fagilimate all zoom and cross?”
 - A. is something a schizophrenia patient might say
 - B. is something a person with abnormalities of the frontal and temporal lobes might say
 - C. is something that a patient taking a dopamine agonist might say
 - D. patient would be helped by taking a neuroleptic drug
 - E. all are **TRUE**

6. Damage to the prefrontal cortex (all parts included) results in:
- A. inappropriate affect
 - B. perseveration
 - C. intellectual decline
 - D. problems with working memory
 - E. three of the above
7. Hallucinations, perceptual distortions, and altered sensory experiences can be elicited by:
- A. high doses of dopaminergic antagonists
 - B. high doses of carbachol (cholinergic agonist)
 - C. high doses of MHPG (major metabolite of NE)
 - D. high doses of alpha-2 NE autoreceptor agonists
 - E. high doses of dopaminergic agonists
8. Some of the structural abnormalities associated with schizophrenia include:
- A. ventricular enlargement, decreased volume of medial temporal lobe structures, and altered pattern of cellular arrangement in temporal and frontal brain regions
 - B. ventricular enlargement, increased hippocampal volume, and altered pattern of cellular arrangement in temporal and frontal brain regions
 - C. ventricular shrinkage, increased temporal lobe volume, and altered pattern of cellular arrangement in the entorhinal cortex
 - D. ventricular enlargement, decreased temporal lobe volume, and increased frontal cortical volume
 - E. decreased temporal lobe volume, decreased frontal lobe volume, and under activity of dopamine in these regions
9. Antipsychotic drugs are thought to exert their beneficial effects via:
- A. blockade of the alpha₂ NE autoreceptors
 - B. decreasing the effects of physostigmine
 - C. blockade of dopaminergic receptors
 - D. blockade of clonidine receptors
 - E. blockage of DA release in visual cortex
10. Which of the statements below is **TRUE** regarding the following sentence? “He strode across the court and protested vigorously that his opponent was infringing upon the rules by using an illegally strung tennis racket.”
- A. lesions of a higher visual cortical area (19 for example) would affect one’s ability to know that the “court” refers to a tennis court rather than a court of justice
 - B. immediately after reading the sentence, Phineas Gage would not have been able to understand that the “court” refers to a tennis court rather than a court of justice
 - C. immediately after reading the sentence, you are using your PFC to understand that the “court” refers to a tennis court rather than a court of justice
 - D. none of the above is/are **TRUE**
 - E. two of the above are **TRUE**

11. Which of the statements below is **FALSE** regarding the prefrontal cortex (PFC)?
- A. targeted by DA neurons in the VTA
 - B. is supplied by anterior and middle cerebral arteries
 - C. receives inputs from the mediodorsal (MD) of the thalamus
 - D. is interconnected with the amygdala, hypothalamus, and hippocampus
 - E. lies caudal to supplementary motor cortex (SMA) and lesions result in apraxias
12. Which of the statements below is **TRUE**?
- A. in a working memory task, some cells in the dorsolateral PFC increase their firing during the period when the target stimulus needs to be “kept in mind”
 - B. infant monkeys, and monkeys with lesions of the dorsolateral PFC, would have difficulty keeping the location of the target “in their mind”
 - C. a monkey with abnormally high levels of DA in the dorsolateral PFC would have difficulty keeping the location of the target “in mind”
 - D. a short order cook with abnormally high levels of DA, and no pencil, would have trouble keeping your order “in mind”
 - E. all of the above are **TRUE**
13. Which of the statements below is **TRUE**?
- A. patients with lesions of the dorsolateral PFC would have difficulty on the Wisconsin Card Sort Test (WCST)
 - B. lesions of the dorsolateral PFC result in perseveration
 - C. schizophrenics exhibit decreased blood flow in the dorsolateral PFC during the WCST
 - D. schizophrenics engage in repetitive behaviors
 - E. all of the above are **TRUE**
14. Which of the following statements is **FALSE**?
- A. patients with lesions localized to the orbital and medial aspects of the PFC exhibit normal intellectual function
 - B. patients with lesions localized to the orbital and medial aspects of the PFC (Phineus!) often appear “bland”
 - C. patients with lesions localized to the orbital and medial aspects of the PFC can form new memories
 - D. patients with lesions localized to Wernicke’s area of the temporal lobe can comprehend and exhibit a fluent aphasia
 - E. patients with bilateral lesions of the hippocampus can not form new memories

15. Which of the following statements is **FALSE** regarding the temporal lobes?
- A. have interconnections with parietal and frontal lobes
 - B. have interconnections with hypothalamus and amygdala
 - C. contain the hippocampus, parahippocampal gyrus, fornix, Wernicke's area and primary auditory cortex (41 and 42)
 - D. lesions result in Capgras syndrome, which is when you think the workers you know with Lawn Care Inc. are "imposters" (get it?)
 - E. involved in "Executive" functions

16. Temporal lobe epilepsy (TLE):
- A. patients may experience major motor convulsions typical of a grand mal seizure
 - B. patients may experience seeing a face, a scene and hearing a voice or music; they also might experience a past event in vivid detail (auditory and visual hallucinations)
 - C. patients may experience gustatory (taste) hallucinations
 - D. patients may experience memory flashbacks, "out of body" experiences or feelings of emotion such as fear or pleasure
 - E. three of the above are **TRUE**

17. Hallucinations:
- A. occur in schizophrenia
 - B. are associated with changes in parietal lobe glucose metabolism
 - C. are associated with malfunctioning of the **right** hemisphere over/near areas 41 and 42
 - D. in patients with auditory hallucinations auditory evoked potentials in areas 41 and 42 exhibit decreased latencies (get their faster!)
 - E. none of the above are **TRUE**

- 18 Neuroleptics:
- A. reduce the effects of serotonin
 - B. are given to patients with low dopamine levels
 - C. block norepinephrine receptors
 - D. affect only the dopamine receptors in the frontal and temporal cortex
 - E. act as dopamine antagonists

PROBLEM SOLVING ANSWERS

1. C
2. C
3. D
4. E (B, C, D)
5. E
6. E (A, B, D)
7. E
8. A
9. C
10. C
11. E
12. E
13. E
14. D
15. E
16. E (B, C, D)
17. A
18. E