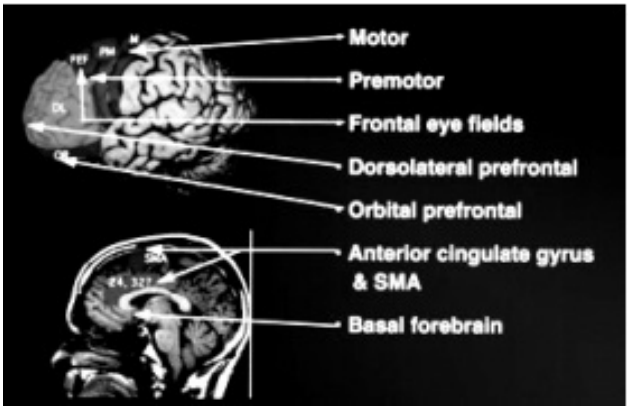
Regions of the Frontal Lobes

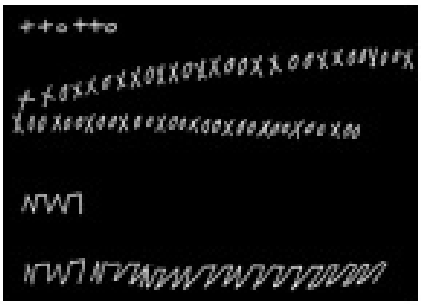


1. ***Primary Motor Cortex (M1, Brodmann area 4):*** The primary motor cortex is located on the precentral gyrus just rostral to the central sulcus. It is the source of cortical neurons that will project to the brainstem and spinal cord to activate neurons involved in the control of voluntary movements. It receives input from the neighboring **primary somatosensory area** (S1, on the postcentral gyrus) and **premotor cortex**, as well as from the **ventral lateral nucleus** of the thalamus (a relay nucleus with projections from the cerebellum). These inputs modulate the output of M1 by providing information about the positioning, timing, and coordination of voluntary movements. The output of M1 goes by way of the **internal capsule** to synapse in the brainstem (the projection referred to as the corticobulbar tract) or the spinal cord (the corticospinal tract). Damage to M1 will cause **contralatereral motor deficits**, initially a flaccid hemiplegia/hemiparesis and later a spastic hemiplegia/hemiparesis. Depending on the extent of cortical damage, these deficits may be localized to a specific region of the body or can be more widespread.

2. ***Premotor Cortex (BA6):*** The premotor cortex is located immediately rostral to M1. Its primary function is to assist in integration of sensory and motor information for the performance of an action (praxis). Thus it receives input from **secondary somatosensory area** (immediately caudal to S1 in the parietal cortex) and the **ventral anterior thalamic nucleus** (a relay nucleus with projections from the basal ganglia, which themselves are a group of subcortical nuclei that modulate motor activity). The output of premotor cortex is to **M1** and **contralateral premotor area** (by way of the corpus callosum). Damage to premotor cortex may result in (1) **apraxia**, an acuired inability to carry out skilled actions that could previously be performed (but without paralysis); (2) **deficits in contralateral fine motor control,** such as the performance of complex serial movements; and (3) **difficulty in using sensory feedback** for the control and performance of movements.

3. ***Frontal eye fields (BA8):*** The frontal eye fields are located rostral to premotor cortex. Their primary function is associated with control of voluntary eye movements in the contralateral visual field for processes such as active visual search. Their connections

with the rest of the brain are complex and beyond the scope of this discussion. Damage to the frontal eye fields will cause **deficits in voluntary eye movement** to the contralateral visual field (leading to active visual search deficits), but preserved passive eye movement (as in the following of a moving object).

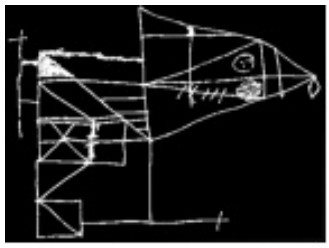


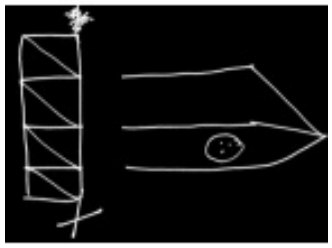
4. ***Dorsolateral prefrontal cortex (BAs 45-49):*** The dorsolateral prefrontal cortex makes up the largest proportion of frontal cortex, located rostral to the frontal eye fields and superior to orbitofrontal cortex. The functions of this region of the brain fall under the heading of "**executive**" processes, which in a general sense involves the ability to utilize sensory input from multiple modalities (ie. visual, auditory) in generation of appropriate responses. Its connections with the rest of the brain are extensive, but one circuit of considerable importance involves input from the **thalamus** (primarily ventral anterior and mediodorsal nuclei) and output to the **caudate** nucleus of the basal ganglia (this circuit will be described in greater detail later). The function of the dorsolateral cortex is probably best reflected in the tasks used to assess dysfunction of this region. There are several tests currently in use that aim to qualitatively characterize deficits of the dorsolateral cortex.

a. **Figural fluency tasks:** Patients are asked to draw as many different shapes as possible within a limited time period. Patients with dorsolateral dysfunction might get "stuck" on one shape and continue to draw either the same figure or something very similar (an error called **perseveration**). Here one can observe that the patient is having difficulty generating **multiple response alternatives**.

b. **Luria's Alternating Figures Test:** Patients are asked to copy a sequence of alternating +'s and 0's and then to continue the pattern across the page (top image). Patients with dorsolateral dysfunction may persist in drawing only +'s or only 0's (perseveration), or they may change the task entirely and begin drawing x's (exhibiting **impersistence** in completion of the appropriate task). Again one can note difficulty in **generating appropriate responses** to the task at hand. Note that similar tests to assess errors of this sort may be performed using alternating hand movements or the drawing of different patterns of peaks and valleys (bottom image).

c. **Visual Organization Test:** Patients are presented with pictures of common objects that have been cut apart and rearranged on the page like a puzzle. A patient with dorsolateral dysfunction will not be able to "piece" back together the cut-apart object, instead focusing on a single aspect of one of the shapes on the page. Here **difficulties in integration of sensory information** are especially apparent.

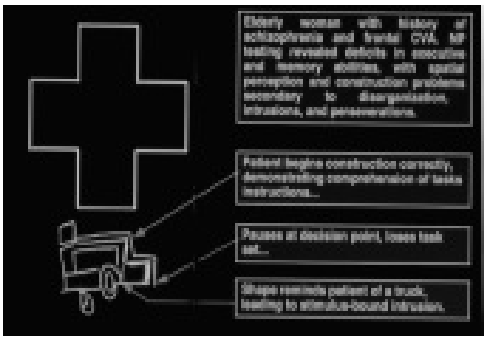




d. **Copy/Free Recall Tests:** Patients are presented with a figure that is first to be copied (top image) and then later to be drawn from recall (bottom image). When drawing from recall, patients with dorsolateral dysfunction will remember to draw certain details of the figure without regard for the general shape and organization of the figure as a whole. This deficit reflects **poor organization of learning and recall** in these patients.

5. ***Orbitofrontal Cortex (BAs 10-14):*** The orbitofrontal cortex is located inferior to dorsolateral prefrontal cortex in the most rostral portion of the frontal lobe. It has several functions, including the **modulation of affective and social behavior**, **working memory for feature information**, and **smell discrimination**. The orbitofrontal cortex receives input from **limbic and olfactory systems**, along with **inferotemporal lobe** areas (memory formation), **and ventral visual pathways** (analysis of form and color of visual input). Its output is to autonomic musculature and the basal forebrain cholinergic system (both targets are involved in regulation of behavior). General observation of patients exhibiting **behavioral disinhibition** or **socially inappropriate actions** might suggest orbitofrontal deficits, particularly if on neurological exam the patient also exhibits anosmia (an inability to discriminate smells). Tests of orbitofrontal dysfunction are fewer in number than those used to assess dorsolateral problems:

a. Drawing tasks may show **disinhibition and intrusion** in the construction of figures and shapes for a patient with orbitofrontal dysfunction.



b. The "go/no-go" task requires patients to make a response to a "go" signal and withhold a response to a "no-go" signal. The task is often made more difficult by changing the habitual meaning of the signals (ie. the patient is instructed to tap their

fist when the examiner says "stop" and not tap when the examiner says "go"). A patient with orbitofrontal dysfunction will have difficulties **inhibiting their behavior** during these tasks.

6. ***Cingulate Cortex/Supplementary motor area (BAs 24, 32):*** The cingulate cortex is located in the medial portion of the cortex just superior to the corpus callosum. The supplementary motor area is located medial to the premotor cortex just anterior to M1. These regions of the brain have functions that are involved with **drive and motivation** along with **environmental exploration**. Their connections are with **deep limbic structures** of the brain (ie. basal forebrain structures such as the nucleus accumbens). Dysfunction in the cingulate/SMA are associated with several uniquely bizarre characteristics, **including apathy and akinetic mutism** (reflecting a loss of drive and motivation) along with **complex attentional deficits** and **delayed habituation** to external stimuli. The **alien hand syndrome** may also be present, whereby patients report experiencing a loss of conscious control over the movements and actions of their hand, which proceeds to "explore" the surrounding environment by, for instance, unbuttoning clothes.

Frontal: Subcortical Connections

The frontal cortex has connections to subcortical structures such as the thalamus and basal ganglia that function in regulation of behavior. As alluded to earlier, the dorsolateral prefrontal cortex is a part of a circuit with input from the **thalamus** and output to the **striatum** (a basal forebrain nucleus). The striatum then projects to **globus pallidus/substantia nigra** (another basal forebrain structure), which projects to the **thalamus** to complete the circuit. Other parallel but distinct connections exist between the orbitofrontal/cingulate frontal regions and their corresponding subcortical structures. In a very general sense, the frontal:subcortical:frontal circuits may be thought of a "filter" that serves to modulate the output of the frontal cortices to regions of the brain involved in motor control of behavior. **Small subcortical lesions** that affect any one of these circuits can **mimic large cortical lesions**.

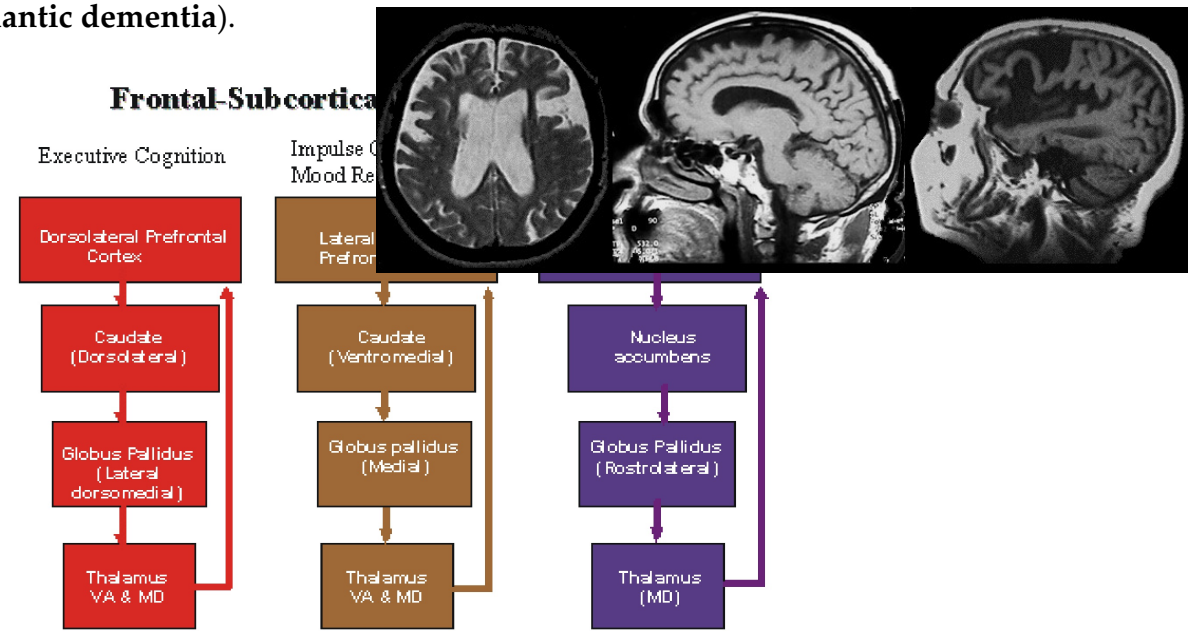
Frontal Cortex ⇨ Striatum ⇨ Globus Pallidus/Substantia Nigra ⇨ Thalamus ⇨ Frontal Cortex

Disorders Associated with Frontal Lobe Dysfunction

Frontal lobe dysfunction may be found in a host of disorders ranging from cortical degenerative disorders often seen in the elderly, including Alzheimer's Disease and Fronto-Temporal Lobar Dementia, to disorders of a psychiatric nature (schizophrenia, obsessive compulsive disorder). As noted above, subcortical damage can also result in frontal dysfunction; such damage may be seen in disorders of basal ganglia nuclei such as Huntington's Disease and Parkinson's Disease. Some representative examples of disorders associated with frontal lobe dysfunction are as follows:

1. **Fronto-Temporal Lobar Degeneration:** This is a degenerative disorder of the cerebral cortex that preferentially affects the frontal and temporal lobes of the brain. The symptoms exhibited by patients with fronto-temporal lobar degeneration are reflected in the brain areas affected.

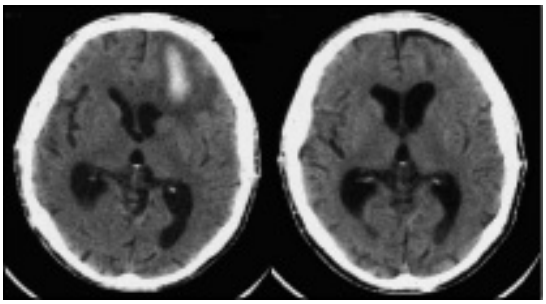
a. **Orbitofrontal** dysfunction may cause **behavioral disinhibition.**
b. **Cingulate** deficits may cause **apathy**.
c. **Dorsolateral** deficits may cause problems with **executive** functions.
d. **Temporal lobe** lesions may adversely affect the amygdala (a structure involved in **emotional processing and social behavior**) or the left temporal lobe (associated with language functions—deficits can result in **aphasia, semantic dementia**).



The deficits associated with frontotemporal dementia (FTD) may be contrasted with

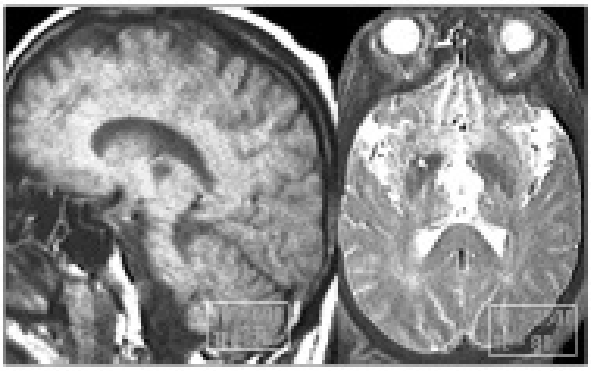
those of Alzheimer's disease (AD), another cortical degenerative disorder that preferentially affects the temporal lobes (specifically the hippocampus). While FTD may be associated with early dysfunction in behavior/personality and executive functioning, **Alzheimer's patients** will show **preservation of personality and behavior** while exhibiting **deficits more specific to memory function**. Cortical patterns of atrophy, visualized through brain imaging methods (MRI or CT) will also typically distinguish the frontotemporal degeneration of FTD (seen in the image to the right) from the hippocampal atrophy seen in AD.

2. **Traumatic brain injury:** Blows to the head are especially likely to affect the orbitofrontal poles of the brain, sometimes causing such a patient to exhibit **behavioral disinhibition and inappropriate actions**. The image to the right shows damage to a patient in the orbitofrontal region following trauma.



3. **Schizophrenia:** This is a psychiatric disorder characterized by periods of psychosis (loss of touch with reality) and bizarre behavior interspersed with periods of "negative" symptoms, characterized by flattening of affect (showing no emotions), lack of motivation, social withdrawal, and speech deficiencies. These **negative symptoms** are thought to be due to **decreased neural activity** (mediated by dopamine-secreting neurons) in **dorsolateral prefrontal: subcortical circuits**.

4. **Obsessive-Compulsive Disorder:** This is a disorder whose patients have recurrent unwanted, intrusive thoughts (obsessions) that cause anxiety; the anxiety is relieved to some extent by performing repetitive actions (compulsions). **Overactivity** in **frontal:subcortical circuits** is thought to be central to the pathogenesis of this disorder, and surgical treatment for refractory (resistant to treatment) OCD involves the interruption of these circuits.



5. **Korsakoff's dementia:** Korsakoff's dementia is a disorder caused by a **deficiency of vitamin B1 (thiamine)** and often occurs in chronic alcoholics (since alcohol serves as a substitute for foods with

essential nutrients). The disease is characterized by **severe amnesia** and causes degeneration of the medial thalamus, mamillary bodies, and cerebral atrophy in regions such as the frontal lobes (see image below). Patients with Korsakoff's dementia often exhibit many of the same neuropsychological deficits that are seen in other frontal patients.

Other Indicators of frontal lobe dysfunction

1. **Working Memory Tests:** Working memory tests are often used to evaluate frontal lobe function in patients. Some of the more common working memory tests include:
a. **Spatial working memory tasks:** An example would be a **delayed response task**, which might require a patient to take note of the position of a dot that briefly flashes on a screen, withstand a variable delay in which they are asked to perform another task, and then after this delay point to the position where they remember seeing the dot (hence testing the ability to remember the spatial position of the dot). Another test of spatial working memory, which also is able to detect perseverance errors, is **delayed alternation**.
b. **Feature working memory tasks:** An example would be a **delayed matching to sample** task, which might require a patient to view a figure presented briefly on a screen, withstand a variable delay in which they would be shown a number of other figures, and then after this delay have to identify the original figure when presented among several choices. **Delayed object alternation** is a variant on this test that, like spatial delayed alternation, assesses the presence of perseverance errors.

2. **Reflexes:** Patients with frontal lobe dysfunction may exhibit reflexes (often referred to as "release signs") that are present in infancy but disappear with normal development. These include the **snout**, **suck**, **glabellar**, and **grasp** reflexes.

3. **Dystonias:** Patients with frontal lobe lesions may exhibit **gegenhalten**, a behavior in which resistance to movement of a limb increases throughout flexion and extension. This phenomenon should be distinguished from **cogwheeling**, which is another dystonia characterized by ratchet-like movements of joints and is characteristic of Parkinson's disease.

4. **Gait abnormalities:** Patients with frontal lobe dysfunction may exhibit characteristic abnormalities in gait, such as difficulty in picking their feet up off the ground when they ambulate (**magnetic gait**).