

THE PREFRONTAL CORTEX

Connections

Dorsolateral Frontal Cortex (DFPC)

Inputs

The DFPC receives inputs predominantly from somatosensory, visual and auditory cortical association areas in the parietal, occipital and temporal lobes.

The DFPC is strongly included in re-entrant basal ganglia-thalamocortical circuits that involve parts of the basal ganglia which are, among others, projected upon by parietal, occipital and temporal association cortices.

The processing of information in the DFPC is modulated by cholinergic and monoaminergic inputs from the basal forebrain and brainstem. These latter cell groups, in turn, are influenced by inputs from the orbitomedial PFC.

Outputs

The outputs of the DFPC are directed towards the premotor cortex, as well as to the somatosensory association cortices, from which it receives information, probably providing these sensory areas with feed-forward information about motor/behavioral commands.

A further output of the DFPC may reach brainstem structures like the deep layers of the superior colliculus, the midbrain tegmentum, and the dorsolateral part of the PAG.

Orbitomedial PFC (OPFC)

Inputs

The OPFC also receives inputs from somatosensory, visual and auditory association areas, but to a much lesser extent than the DFPC; the recipient area is restricted to the lateral and caudal parts of the OPFC. However, inputs from olfactory, gustatory and visceral sources are much more prominent and widespread.

The OPFC receives strong inputs from the basal amygdaloid complex and the parahippocampal cortices; inputs from the hippocampus proper reach predominantly the medial wall of the PFC.

Outputs

The OPFC is involved in re-entrant basal ganglia-thalamocortical circuits that involves parts of the basal ganglia (BG) which are innervated by limbic structures such as the hippocampus and amygdala as well as by limbic associational cortices.

There is a reciprocal relationship between the OPFC and the cholinergic cell groups in the basal forebrain and the monoaminergic cell groups in the brainstem and hypothalamus. Through these projections the OPFC may influence the cholinergic and monoaminergic innervation of widespread cortical and subcortical regions of the forebrain.

The OPFC further projects to the lateral and posterior hypothalamus, in this way reaching stress and autonomic centers in the brain.

In addition, direct brainstem projections reach the ventrolateral part of the PAG, the peribrachial region, the NTS, and the dorsal motor nucleus of the vagus, all involved in autonomic functions. Prefrontal fibers even extend to the spinal cord.

In conclusion, the organization of the anatomical connections of the PFC signifies its integrative position in relation to the somatosensory, viscerosensory, somatomotor and visceromotor, cognitive and limbic systems in the brain.

FUNCTIONS OF THE PFC

Goal-oriented behavior. The PFC has key role in organizing goal-oriented behavior. One must identify a goal; develop subgoals. In choosing among the goals, consequences must be anticipated. Complex actions require that we shift from one subgoal to another in a coordinated manner. One must determine what is required to achieve the subgoals. There are often competing goals, the situation may require a response that competes with a strong habitual response, the situation need troubleshooting, or the situation is dangerous or novel, etc. For a person engaged in goal-oriented behavior, especially in a behavior that involves subgoals, it is important that there be a way to monitor progress. Patients with frontal lobe lesions are aware of their deteriorating social situations and have the intellectual capabilities to generate ideas that may alleviate their conditions. But their efforts to overcome their inertia are haphazard at best. They are unable to sustain a plan of action and meet their goals. How the PFC achieve these functions? 1) Represent and maintain information that is essential; 2) Guide task selection and switching tasks; 3) Monitor progress

Working memory: Working memory is essential for representing information that is not immediately present in the environment. It allows for the interaction of current goals with perceptual information and knowledge accumulated from past experience. Not only we must be able to represent our goals, but also is essential that these representations persist. Working memory is not only about keeping

task-relevant information active; it is also about manipulating that information to accomplish behavioral goals. One of the basic physiological capacities of neurons in the DPFC would be their ability to hold, during a certain delay period between a (sensory) stimulus and the (motor) reaction, sensory (somatosensory, visual, auditory) information 'on line' in order to use this information for the guidance of behavior independent of the immediate stimuli. Although neurons in other parts of the cortex may exhibit similar physiological characteristics, it seems very likely, that this capacity of PFC neurons is very important in the adequate selection of behavioral responses, aspects of rule learning (Passingham), decision-making process.

The psychological model of executive control. The Supervisory Attention System of Shallice. The monitoring System. PET and fMRI imaging studies suggest that the anterior cingulate cortex occupies an upper rung in the attentional hierarchy and ensure interactions among working (in the prefrontal) selection-operation (prefrontal) and long-term memory systems (in the posterior cortex). The cingulate cortex works as a conflict monitoring system, recruits and allocate necessary attentional resources. The PFC, including the anterior cingulate cortex, participate in amplification of representations that are useful for the task and ignore potential distractors. (allocation of attentional resources; dynamic filtering). Frontal lobe patients display heightened interference on the Stroop task (Failure to inhibit irrelevant information) and show perseveration in the: WCST test (Failure to flexible shifting of goals). It is now clear that the basal ganglia are not only the recipient of PFC inputs but also project to the PFC. In view of the strong inhibitory nature of the basal ganglia projections to the thalamocortical systems in 'resting' conditions, the PFC has an important role with the BG in behavioral response selection.

Rule representation. Miller and Cohen (2001) proposed that reward signals from midbrain dopamine systems act on the multimodal circuitry of the PFC to strengthen connections between neurons that process the information that led to the reward. Maintenance mechanisms in the PFC sustain a circuitry among sensory, motor and mnemonic representations. The PFC produces a feedback signal to the posterior cortex that bias the flow of information along lines that match the PFC representation, ie. along a task-relevant neural pathways. In short, the PFC design a map of which neural pathways in the forebrain are successful at solving a task and then holds it on-line in the PFC so that the rest of the neocortex can follow it. Behavioral and neurophysiological studies also point to the operation of top-down signals on the visual cortex, presumably coming from the PFC that enhances representations of behaviorally relevant stimuli at the expense of irrelevant ones.

Multiple Processing Levels in the Prefrontal Cortex. The lateral PFC is conceptualized as a working memory system devoted to sustaining representations of information stored in the cortex's more posterior region through selection mechanisms. The anterior cingulate is hypothesized to work in tandem with PFC, monitoring operations of this system (Gazzaniga, 2002). Petrides (1998) proposes a two-tier system in the primate lateral frontal cortex (Fig.). Accordingly, the ventrolateral PFC receive inputs from the sensory cortex

and is responsible for their simple maintenance in working memory and for retrieval of information from long-term memory. The dorsolateral PFC takes this information and performs more executive functions, such as monitoring multiple behaviors and manipulating information. For example, simple rehearsing a phone number is a ventrolateral PFC function while saying the same number backward is a dorsolateral PFC function.

Social-emotional decision making. The role of the OPFC should be considered in the context of its extensive reciprocal relationships with limbic and autonomic structures. First, the reciprocal relationships with limbic structures, such as the hippocampus and amygdala, provides the PFC with the possibility to gain access to the memory and emotional processes in which these temporal lobe structures are involved, in this way, past experience can be brought 'on-line' and may play a role in guiding complex behavioral processes. Second, the reciprocal relationships with the hypothalamic and autonomic systems would provide the OPFC with information about the bioregulatory responses that take place or have taken place in the past in the course of cognitive and socio-emotional decision making processes. This forms the basis for the 'somatic marker' hypothesis which proposes that signals from bioregulatory responses, that are aimed at maintaining homeostasis and ensuring survival, are essential for decisions in complex socio-emotional behavior settings. In this way, emotion may have a profound influence on the cognitive functions of the brain. As suggested by Damasio and his coworkers "...too little emotion has profoundly deleterious effects on decision making: in fact too little emotion may be just as bad for decision making as excessive emotion has long been considered to be." The orbitofrontal cortex seem to be especially important for processing, evaluating, and filtering (inhibiting) social and emotional information. Damage to this region impairs the ability to make decisions that require feedback from social or emotional cues. In some situations, the responses of patients with orbitofrontal lesions seem overly dependent on perceptual information, ignoring social cues, expectations. Further evidence of the reliance on external cues is that some orbitofrontal patients are prone to imitative behaviors. They often show a change in personality, irresponsibility, and lack of concern for the present or future. A similar loss of social guidance of behavior can be observed in primates after they receive lesions to their prefrontal cortex. The social status of animals that receive lesions of the orbitofrontal cortex plummets immediately. It is not clear, however, what cues the healthy animals use to reject the lesioned animals so quickly. At times, patients with damage to this region have difficulty inhibiting inappropriate social responses, such as aggressive impulses. Their actions are more often harmful to themselves than others. The role of the OFC in evaluating social cues also has been linked to antisocial behavior.

According to Edmund Rolls, the OFC is important for the on-line, rapid evaluation of the stimulus-reinforcement associations. At times, deciding on an action requires that we correct stimulus-reinforcement associations when they

become inappropriate based on new information (reversal learning of stimulus-reinforcement association).

The OFC is the central structure of Damasio's somatic marker hypothesis. An upcoming decision calls for activating representations of similar events experienced in the past. Damasio argued that affective memories are essential for rational decisions. They allow us to sift through options, alert us to plans linked to negative feelings, and bias us toward ones connected with positive feelings ('gut feeling'). Somatic markers rapidly narrow the options by automatically anticipating the affective consequences of each action. When the OFC is damaged, the representations required to guide an action are brought into the working memory, but they are stripped of emotional content. Patients with damage to this system might be unable to reach a decision because they become incapacitated by contemplating irrelevant information. None of the outcomes of their actions will be obviously more emotionally preferable than alternative outcomes, and patients might make decisions randomly or impulsively, and as such appear to be disinhibited. A deficient somatic marker system would explain the impairments that patients with damage to the OFC exhibit on the gambling task. The somatic marker hypothesis is somewhat similar to the theory advanced by William James. He proposed that emotional feelings depend on feedback from the autonomic system (see also in the AMYGDALA chapter). A problem with simply using autonomic nervous system signals to identify emotional states, however, is that autonomic states associated with different emotions can be identical. It is perhaps that there is a conditioned association between the autonomic state and various cortical representations.