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The Prefrontal Cortex: A Basic Embryological, Histological, Anatomical, and Functional Guideline

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Abstract

The prefrontal cortex (PFC) unites, processes and controls the information coming from cortex and subcortical structures, and decides and executes goal-oriented behavior. A major function of PFC is to maintain the attention. Furthermore, it has many other functions including working memory, problem solving, graciousness, memory, and intellectuality. PFC is well developed in humans and localized to the anterior of the frontal lobe. This article presents a systematic review and detailed summary of embryology, histology, anatomy, functions and lesions of PFC.

Introduction

The prefrontal cortex (PFC) is the largest cortical area in the human brain, making up 29% of the whole cerebral cortex. It is located in the frontal lobe, anterior to the primary motor cortex and the premotor cortex. PFC has key roles in defining personality and behavior. It also has many functions including maintaining attention, planning complex movements, controlling emotions, discriminating between good and bad, speech, memory, temporal perception and working memory [1-9].

Embryology

The nervous system in humans first emerges at the beginning of the third gestational week as a neural plate as part of the ectodermal plate. At the fourth week, three dilatation areas called the primary brain vesicles form. These are, in order from anterior to posterior, prosencephalon (forebrain), mesencephalon (midbrain), and rhombencephalon (hindbrain) [10].

At the fifth week, prosencephalon divides into two brain vesicles called the telencephalon and diencephalon. At the end of the fifth week, two lateral diverticula develop, which are named as telencephalic vesicles. These two vesicles are the primordial forms of the cerebral hemispheres [10,11].

The developing cerebral hemispheres are initially like three characteristic layers of the neural tube (ventricular, intermediate, and marginal). Later, a fourth layer develops, and the cells in this layer migrate to the marginal layer to form the cortex. The surface of the cerebral hemispheres is initially straight. However, fissures, sulci and gyri begin to form as the brain grows [10,11].

Histology

PFC is comprised of six laminae that cannot be clearly distinguished from each other histologically. From inside to outside, these laminae are:

I. Lamina zonalis: Contains few Cajal horizontal cells. The axons of Martinotti cells located at deep layers, the last branches of the apical dendrites of pyramidal cells, and the last branches of the afferent nerve fibers extend to this lamina.

II. Lamina granularis externa: Harbors granular cells and some small pyramidal cells.

III. Lamina pyramidalis externa: Harbors loosely arranged pyramidal cells, which generally show an increase in size from outside to inside. The axons of these cells traverse the white matter and reach other cortical regions. The axons of these cells make up the ipsilateral and contralateral cortico-cortical connections.

IV. Lamina granularis interna: It is the layer with the highest number of cells. It harbors stellate pyramidal cells and granular cells.

V. Lamina pyramidalis interna: Contains less number of cells in comparison to the other laminae. It harbors well-developed pyramidal cells and Martinotti cells. The axons of the pyramidal cells located in this layer send projection fibers to the basal ganglia.

VI. Lamina multiformis: Harbors Martinotti cells, fusiform cells and pyramidal cells [12,13].

Anatomy

Frontal lobe constitutes the whole cerebral cortex area anterior to the central sulcus. It has three parts. The narrow area anterior to the central sulcus is primary motor cortex (Brodmann 4), and the area immediately anterior to the primary motor cortex is premotor cortex (Brodmann 6). PFC comprises the anterior part of the frontal lobe, located anterior to the premotor cortex [7,14].

PFC is made of the superior frontal gyrus, medial frontal gyrus, most part of the inferior frontal gyrus, a great portion of the part of superior frontal gyrus and frontal gyrus that is on the inner surface of the hemisphere, and anterior part of cingulate gyrus (Figure 1) [15].

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There are three parts of PFC, namely the lateral PFC, medial PFC and orbital PFC (orbitofrontal cortex).

I. Lateral prefrontal cortex: It is comprised of Brodmann's areas 8, 9, 10 and 46. Additionally Brodmann's areas 44, 45 and 47 are also included in the lateral PFC (Figure 2) [17-19]. In literature, some sources cite Brodmann's areas 45 and 47 as ventrolateral PFC, and Brodmann's areas 9 and 46 as dorsolateral PFC. Additionally, the frontal pole, which is the most anterior part of the frontal lobe and is Brodmann's area 10, is named as rostral or polar PFC [20-22].

II. Medial prefrontal cortex: The medial PFC includes Brodmann's areas 8, 9, 10 and 12, and Brodmann's areas 14, 24, 25 and 32 that are located anterior to cingulate gyrus (Figure 3) [17,23].

III. Orbital prefrontal cortex [orbitofrontal cortex]: Brodmann's areas 11, 12, and 13 constitute the orbital PFC (Figure 3). Orbital PFC is anterior to the PFC and surrounds the medial orbital sulcus and lateral orbital sulcus [17,21,22].

Functions of prefrontal cortex

The principle function of PFC is to plan and execute behaviors [24]. PFC collects information from cortex and subcortical structures, and arranges and controls this information; decides and executes the behavior [8].

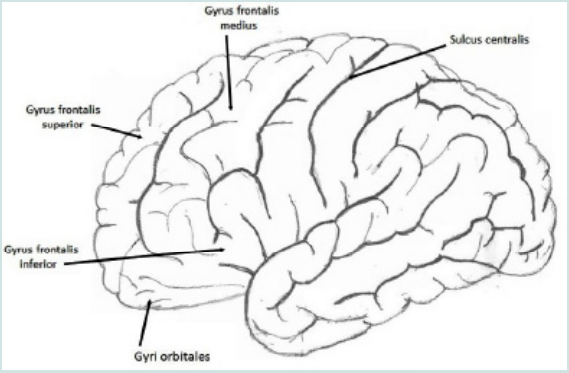

Figure 1: Superior, medial and inferior frontal gyri, and orbital gyri (Drawing modified from Putz R) [16].

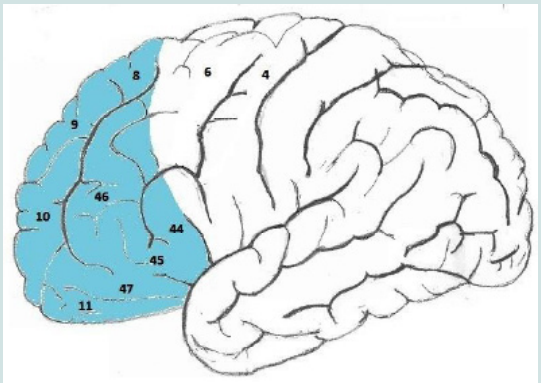

Figure 2: Lateral view of Brodmann's areas 8, 9, 10, 46, 44, 45 and 47. (Pencil drawing modified from Putz R) [16].

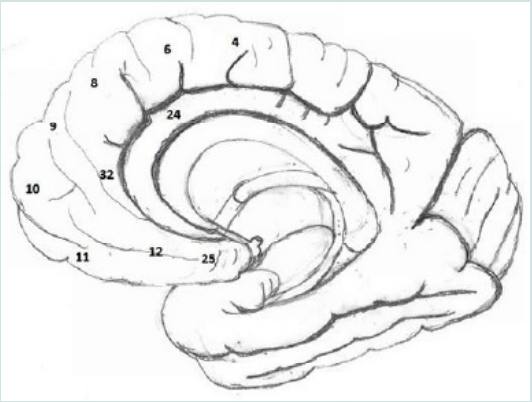

Figure 3: Medial view of Brodmann's areas 8, 9, 10, 11, 12, 24, 25 and 32 (Pencil drawing modified from Putz R) [16].

PFC has vital functions including thinking, reasoning, prospective planning, conforming to the learned social rules, politeness, accurate decision making for sustaining life and executing these decisions. Additionally, morale motivation, self-control ability, common sense, taking lessons from errors and feeling empathy are among the functions of frontal cortex [19,25-27].

PFC owns a "working memory" feature, which is the ability to follow different kinds of information simultaneously and to immediately utilize this information by combining them with the following thoughts. Another function of PFC is the elaboration of thoughts, that is, developing depth and abstractness to the information [3,4,28].

The working memory of PFC executes the storage of transient memory information, temporal perception, foresight, prospective planning, deciding whether the stimulus is behavioral or not, preparing planned and logical response to the sensory signal, solving complex mathematical, ethical, moral and conscientious problems, and controlling whether behaviors are within moral rules or not [25,27,28]. PFC has been shown to play a key role in remembering old information and recalling new memory [29].

One of the main functions of PFC, particularly the dorsolateral section is the attention. It blocks distracting external stimuli and allows focusing and giving attention to a particular task [1,24]. The main function of Brodmann's area 46 that is included in the dorsolateral PFC is working memory and processing of cognitive information [22,30].

The main function of Brodmann's area 11 that is included in the orbital PFC is processing emotions and values. Brodmann's area 47 that is included in the ventrolateral PFC is functions in feeling empathy, and this area activates during an automatic action. Additionally, Brodmann's area 47 in the left hemisphere plays a key role in wording function [22,30].

Brodmann's areas 14, 24, 25 and 32 that constitute the medial PFC are parts of the limbic system. Due to the connection of medial PFC with the limbic system, it functions in processing and enhancement of memory. Additionally, medial PFC is associated with most high cognitive functions [23].

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Ventrolateral PFC has a critical role in the formation of new episodic memories [31].

Lesions of the prefrontal cortex

PFC is highly developed in humans. The lesions of the PFC can be caused by various reasons including trauma, surgical interventions, infections, toxins, chemicals, narcotic drugs, alcohol and chronic stress [32-42].

The first important reported case with a PFC lesion was Phineas Gage, a railway worker, who had an accident in 1848 that damaged the orbital and medial sections of his PFC. That case had relatively normal speech, memory and motor functions, while there were serious disturbances in personality, behaviors, problem-solving, planning and executing these plans [43].

Following lobotomy, which is surgical resection of the connections between PFC and other brain areas, patients lose their abilities to solve complex problems and to perform several tasks simultaneously. They also lose their ability to plan and moral values [28].

Patients with damaged PFC after accidents or traumas show disturbances in decision-making and effective planning of the next couple of hours, and it is impossible for them to make longer-term plans. Additionally, these patients become untidy, ribald, light-minded, impudent and impolite [33,44].

Drug abuse has been shown to cause structural and functional disorders in PFC. This damage results in impaired cognitive control [35-39]. Crack cocaine has been shown to have toxic effects on PFC and to impair the working memory [38,39,45].

During the newborn period, ischemia due to hypoxia results in atrophy in the PFC, and this leads to impairments in executive functions, such as attention deficit and hyperactivity disorder [46,47].

Chronic stress slows down the maturation of PFC during the developmental period and affects its functions [40].

Toxic chemicals like formaldehyde and toluene have been shown to cause damage in the PFC [48-51].

Humans with damaged orbital PFC and monkeys with a lesion in this area have disturbed emotional and motivating behaviors, forget the learned information and have difficulty in reversal learning [52].

Patients with damaged Brodmann's area 11 which is included in the polar PFC and orbital PFC have similar logical thinking ability with normal individuals in the absence of emotional content, whereas they show selectively impaired logical thinking when emotional content is involved [21].

Alcohol exposure during developmental period causes damage in PFC. The resulting damage causes impairment in deciding and executing behaviors [34].

In conclusion, an individual has to think, plan and decide his/her behaviors in order to continue ordinary life. The centers of these vital functions are the prefrontal cortex, which is located in the frontal lobe and covers a quite large area in the cerebral cortex.

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