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Journal of General Medicine and Clinical Practice
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Review Article

Retrosplenial Cortex - Morphofunctional Characteristics

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Received date: November 26, 2024; **Accepted date:** January 13, 2025; **Published date:** January 20, 2025

Citation: Bon L.I, Maksimovich N.Ye, Flurik S.V, Sitsko A, (2025), Retrosplenial Cortex - Morphofunctional Characteristics, *J. General Medicine and Clinical Practice*, 8(1); **DOI:**10.31579/2639-4162/245

Abstract

Retrosplenial cortex (RSC) is a region of the brain located in the posterior part of the medial cortex. It plays an important role in processes related to spatial navigation, memory, and the processing of contextual information. The main functions of the RSC are:
Spatial navigation: The retrosplenial cortex helps to form and maintain internal maps of the surrounding environment. It integrates information from various sensory modalities and is important for spatial orientation.

Memory and context: This region is involved in contextual memory, helping to store and retrieve information based on the surrounding context. This is especially important for associative learning, where context influences recall.

Connectivity with other brain regions: The retrosplenial cortex interacts with the hippocampus, parahippocampal cortex, and other structures, making it part of a larger network responsible for cognitive functions.

Kew Words: retrosplenial cortex; morphofunctional characteristics; brain

Introduction

Retrosplenial cortex (RSC) is a region of the brain located in the posterior part of the medial cortex. It plays an important role in processes related to spatial navigation, memory, and the processing of contextual information. [5]

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Connectivity with other brain regions: The retrosplenial cortex interacts with the hippocampus, parahippocampal cortex, and other structures, making it part of a larger network responsible for cognitive functions.

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Since the late 19th century, when Brodmann first anatomically identified the retrosplenial cortex, substantial experimental evidence has accumulated to support its function. While the exact role of the RSC has not yet been fully defined, research findings from both human and animal studies clearly point to its important role in spatial cognition.

The RSC is a cortical area that Brodmann designated as separate areas 29 and 30, which in humans form a complex with areas 23 and 31 of the posterior cingulate gyrus. Evidence that the retrosplenial cortex (RSC) may act as an interface between memory retrieval and visuospatial processes has also been described. After damage to the retrosplenial cortex, topographical disorientations and navigation deficits were observed, indicating a strong right hemisphere lateralization of the RSC. Patients with small focal hemorrhages localized in the right retrosplenial area exhibit deficits in orientation and experience significant difficulties with spatial navigation. [6]

The retrosplenial cortex is often the subject of research in a number of experiments studying the physiological features of the brain. The development of electrophysiological recordings in animal models has allowed for a deeper investigation of the involvement of the retrosplenial cortex (RSC) in the neural network underlying spatial navigation. The hippocampus, entorhinal cortex, and retrosplenial cortex are key brain structures involved in the creation of an internal map of the environment. In the brain, location, distance, and direction are represented by place cells, grid cells, and head direction cells, respectively.[7]

Electrophysiological recordings from the RSC in rodents have identified neurons that code for an allocentric representation of location. This small population, about 10% of the cells, is known as head direction (HD) cells. They become active when animals maintain a specific direction in their environment, regardless of their position, and become inactive when the head is oriented in other directions. Allocentric representation of location is a way of encoding spatial information about the relative positioning of objects in relation to each other, rather than to oneself (i.e., egocentrically). In this representation, the coordinates of objects in the surrounding environment are taken into account, which allows understanding where one object is located in relation to another. Studies using lesions, as well as electrophysiological recordings in rodent models, have provided a diverse but sometimes contradictory and inconsistent picture of the role of the retrosplenial cortex (RSC) in memory formation. A major drawback of the lesion approach was its high invasiveness. Irreversible damage to entire structures led to undesirable effects, and the need for recovery after damage could trigger compensatory mechanisms. Pharmacological inactivation only partially addressed this issue, as the nonspecific nature of these interventions, targeting the entire structure, remained problematic. The study of the retrosplenial cortex (RSC) is crucial for understanding a range of cognitive processes, such as spatial navigation, memory, and the processing of contextual information.

In a study investigating the activity of neurons in the retrosplenial cortical area during instrumental food-seeking behavior in rats of different ages, conducted by researchers from the Laboratory of Psychophysiology at the Institute of Psychology of the Russian Academy of Sciences (RAS) and the Laboratory of Functional Neurochemistry at the P.K. Anokhin Research Institute of Normal Physiology, A.G. Gorkin, E.A. Kuzina, and others, it was found that the behavior of old and young rats did not differ significantly. However, older rats were significantly more likely to check empty food trays compared to the adult animals.[8]. Similar results were obtained in a series of repeated comparative studies. A comparison of the average firing rate of neurons during food-seeking behavior revealed a significantly higher level of activity in the RSC neurons of adult animals.[8] These findings are consistent with other studies that also reported a decline in the average firing rate of neurons in the prefrontal cortex with age, as well as a decrease in the proportion of highly active neurons in the hippocampus and sensorimotor cortical areas.

The obtained data led to the suggestion that in old age, during learning, there is less "fine-tuning" of existing experience through the formation of new neuronal specializations compared to earlier stages of life. Additionally, it was proposed that the internal systemic structure of newly formed behaviors becomes more "homogeneous" in older animals.[9]

During training rats on new behavioral tasks, E.A. Kuzina found a significant increase in the proportion of neurons in the retrosplenial cortex that were specialized for behavioral acts related to approaching and pressing a lever, compared to the number of cells specifically active during food-seeking acts in the feeding cycle.[10]

E.V. Loseva, N.A. Loginova, and V.V. Gavrilov noted reactive gliosis in layer V of various neocortical areas in rats that were raised in darkness. The results of the study revealed reactive gliosis in all the areas of the cortex examined, with the most pronounced changes observed in the retrosplenial and visual cortical areas.[11]

Earlier, in the same rats raised under conditions of visual deprivation, it was shown that there was a reduction in the overall thickness of the visual and retrosplenial cortices. A detailed analysis revealed a thinning of certain cortical layers across all the brain areas studied. [12]

From the studies conducted by Ivashkina O.I. and Toropova K.A., it can be concluded that the CA1 area of the hippocampus is specifically involved in the formation and retrieval of associative memory for complex signals from the natural environment. To investigate the neural substrates of this memory, immunohistochemical mapping of the neural expression of the c-fos gene in the hippocampus and associative retrosplenial cortex was conducted. It was found that only the CA1 area of the hippocampus, and not other hippocampal regions or the retrosplenial cortex, is activated during the retrieval of associative memory related to a complex conditioned signal, but not its components. Furthermore, a strong positive correlation was found for the CA1 area between the level of freezing during memory retrieval and the number of neurons activated during this retrieval.[9]

In an experiment conducted by E.A. Kuzina on rats trained in a cyclic food-seeking task involving pressing a lever to obtain food from a feeder, single-neuron activity was recorded during the first two weeks after the behavior was acquired, as well as after 30 sessions of daily repetition. A general trend was observed in the dynamics of the neuronal composition specialized for different acts within the behavioral cycle, with an increase in the time interval after training, regardless of the number of repetitions of the new behavior.[9]

In their studies conducted on mice, K.A. Toropova and D.V. Trochev demonstrated that protein synthesis blockade, both during the exploration of a new environment and during the application of an immediate unconditioned stimulus (US) in a familiar environment, disrupts the conditioned reflex freezing response to that environment. The association of a retrieved memory trace of the environment with the unconditioned stimulus (US) was accompanied by the activation of the transcription factor c-Fos expression in the retrosplenial cortex. The retrosplenial cortex was specifically activated during the subsequent retrieval of associative memory of the environment as well. This activation was not observed in mice with impaired memory. No such differences were found in the hippocampus, where c-Fo's expression was activated during the exploration of the new environment but not due to its association with the US. These results suggest that the retrosplenial cortex may function as an area of the neocortex responsible for forming associations between the environment and an aversive unconditioned stimulus.[9]

Behavioral analysis of animals acquiring the first (drinking) and second (food-seeking) skills, conducted by I.I. Rusak and A.I. Bulava, showed that among animals with individual behavioral differences, there were subjects who did not acquire either the first or the second skill. The average speed of these animals was several times lower, and the total time spent in movement was also significantly reduced. It was found that the number of neurons that changed gene expression in the barrel field of the somatosensory cortex during the formation of the second skill depended on how quickly the animals learned the first "whisker" skill. The number of such neurons differed significantly between these two groups of animals. However, the number of such neurons in the retrosplenial cortex did not show significant differences.

Thus, the conclusion was drawn that the more errors the animals made during the acquisition of skill 1, the more neurons were involved in the reorganization of the old experience from skill 1 when forming the new skill 2..[10].

In 2023, researchers from the Engineering-Physics Institute of Biomedicine at the National Research Nuclear University "MEPhI" (S.A. Gulyaev, L.M. Khanukhova, and A.A. Harmash) conducted a study on the bioelectric activity of the retrosplenial cortex of the brain. The study involved 36 healthy volunteers of various ages who had signed informed consent forms. Of these, 19 participants were under 30 years old, and 17 were older than 30 years. The average age of the participants was 29.1 years.

All participants underwent EEG recordings, including the study of baseline brain activity during passive relaxed wakefulness with closed eyes in a "sitting" position and a similar study in a "lying" position (with monitoring of the onset of physiological sleep). The analysis of alpha activity in occipital and parietal leads, conducted for the entire group, revealed a decrease in alpha activity frequency before falling asleep. Notably, in the group older than 30 years, the decrease in alpha activity frequency before sleep onset was statistically significant. The study also showed that the alpha activity detected during classical EEG studies is not a single "baseline" rhythm characteristic of brain structures but rather a combination of several rhythms with similar frequency-amplitude characteristics. These bioelectrical activities are produced by different brain structures, including the retrosplenial cortex. This finding allowed for a new interpretation of results from studies revealing the heterogeneity of alpha rhythm spectra in individuals with various mental deviations. According to the authors of the study, the use of frequency analysis of brain bioelectric activity in the classical EEG methodology cannot be considered an effective method for investigating higher nervous functions, a conclusion that the authors refuted in their work. [11]

An experiment conducted by Auger SD and Maguire EA, in which male and female participants were asked to read three different types of sentences during an fMRI scan, provided insights into the role of the retrosplenial cortex (RSC). The sentences described either something permanent or transient, with the first two types being imagery-based, focusing either on spatial landmarks or actions, while the third type involved non-imagery-based abstract concepts.

The study showed that the RSC was engaged in processing permanent landmarks and stable, sequential actions, but did not respond to transient landmarks or actions, nor to abstract concepts, even those embodying the idea of stability. The researchers concluded that the RSC may not only assist in mapping spatial environments but also potentially provide information about the reliability of events occurring within those environments. [12]

An analysis of resting-state functional magnetic resonance imaging (fMRI) data from healthy aging participants and patients with subjective cognitive impairment, conducted by Kim NH Dillen, Heidi IL Jacobs, Juraj Kukolja, and others, revealed a connection between the activity of the retrosplenial cortex (RSC) and memory functions, as well as neurodegenerative diseases like Alzheimer's disease. Changes in RSC activity may be one of the earliest signs of dementia. These findings are supported by several other studies. The most notable results regarding RSC function come from studies involving patients with damage to this area of the brain. Patients with RSC damage exhibit a deficit in personal autobiographical memories while retaining overall intellectual function. In a study by Edward Valenstein and Dawn Bowers at the University of Florida, they observed a 39-year-old male patient who developed both retrograde and anterograde amnesia following a hemorrhage from an arteriovenous malformation near the corpus callosum. MRI scans revealed damage to the corpus callosum and the area containing the retrosplenial cortex and cingulate gyrus. Although the fornix was anterior and inferior to the damage and may have been involved, the terminal stripe likely remained intact. Structures critical for memory, such as the hippocampus, thalamus, and basal parts of the anterior brain, were preserved. The retrosplenial cortex receives input from the subiculum and projects to the anterior thalamus, thus providing an alternative pathway between the hippocampus and thalamus. More importantly, medial temporal structures involved in memory receive input from the anterior thalamus directly through the cingulate gyrus and indirectly via relay in the retrosplenial cortex. This thalamocortical part of the Papez circuit is likely crucial for memory, and damage to the cingulate and retrosplenial cortices could disrupt this pathway, leading to amnesia.[14]

A study of taxi drivers navigating through central London in a virtual environment showed complete activation of the retrosplenial cortex (RSC) both during route planning and when making spontaneous decisions to alter their route during navigation. This suggests that the RSC plays a key role in the cognitive processes involved in spatial navigation, particularly in flexible decision-making and the ability to adapt one's route based on changing circumstances. [15]

Thus, the retrosplenial cortex (RSC) is an important part of the brain involved in cognitive processes such as memory, spatial navigation, and context perception. Anatomically, the RSC is located in the cortical area that Brodmann identified as areas 29 and 30, which in humans form a complex with areas 23 and 31 of the posterior cingulate gyrus. The primary functions of the RSC include spatial navigation, memory preservation, and context perception, as well as its connections with other areas of the brain. Although the functions of the RSC are not yet fully understood, this makes the RSC a relevant topic for ongoing research.

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DOI:10.31579/2639-4162/245