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Interhemisphere Asymmetry in the Structure of the Hippocampus in Men

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Objectives. To study the cytoarchitectonic structure of the hippocampus in men in the left and right hemispheres. **Materials and methods.** Continuous series of total frontal sections of the cerebral hemispheres were studied in the brains of four men aged 19–30 years. Specimens were stained with cresyl violet by the Nissl method and analyzed using image analysis software. **Results.** The characteristics of the field profile of pyramidal neurons in field CA1 were determined, along with the distribution density of neurons and glial cells in the left and right hemispheres of male brains. The dimensions of the field profile of pyramidal neurons in hippocampal field CA1 in the right hemisphere were larger and their distribution density was lower as compared with the left hemisphere. Field CA1 in the right hemisphere of men's brains had greater density of total glial cells and a higher ratio of satellite glial cells to the total number of glial cells as compared with the left hemisphere. **Conclusions.** The gender-related characteristics of the structural organization of the hippocampus in men evidently correlates with the properties of memory in men.

Keywords: brain, man, cytoarchitectonics, field CA1, hippocampus.

The challenge of memory in neurobiology is fundamental, because of increases in longevity and the numbers of elderly people. Thus, the prevalence of diseases such as senile dementia, Alzheimer's disease, and vascular dementia, all of which involve memory impairments, is increasing [8–10]. This generates the need to study the structural organization of the hippocampus of the human brain, which is the basic cytoarchitectonic formation with which short-term and long-term memory are associated [4], and the recall of information relating to past events.

The hippocampus plays a major role in the ability of humans to orient themselves in space, determining position and the route to a specified target and supporting the ability to recall information relating to the topography of a place and the surrounding space [15, 16].

The hippocampus has a complex cytoarchitectonic structure. It includes five cytoarchitectonic fields: CA1, CA2, CA3, CA4, and CA5, along with the dentate fascia. The main layer in the hippocampus is the pyramidal layer, which consists of efferent pyramidal neurons [1, 3, 11, 25].

The literature lacks data on interhemisphere asymmetry and the cytoarchitectonic organization of the hippocampus of the human brain.

The aim of the present work was to study the cytoarchitectonics of hippocampal field CA1 in men.

Materials and Methods. Frontal sections of eight cerebral hemispheres from men aged 19–30 years were studied; subjects died from causes unrelated to brain pathology. All men were right-handed. The study was approved by the ethics committee of the Neurology Science Center (Protocol No. 6/15 of June 10, 2015).

Brains harvested from skulls were placed in a container with 10% formalin for three days, after which the vascular meninges were removed. The brain stem and cerebellum were transected at the boundary of the cerebral peduncles and each hemisphere was cut on a microtome (Sartorius Werke, Germany) into five equal blocks about 3.5 cm thick, which were immersed in 10% formalin for 7–10 days, after

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TABLE 1. Study Time Points, days

Ethanol							Chloroform		Paraffin			
60°	70°	80°	96° I	96° II	abs. I	abs. II	I	II	44–48°	46°, 46–48°, 50°, 50–52° melted		
10	10	10	10	7	6	4	4	3	1	1	1	1

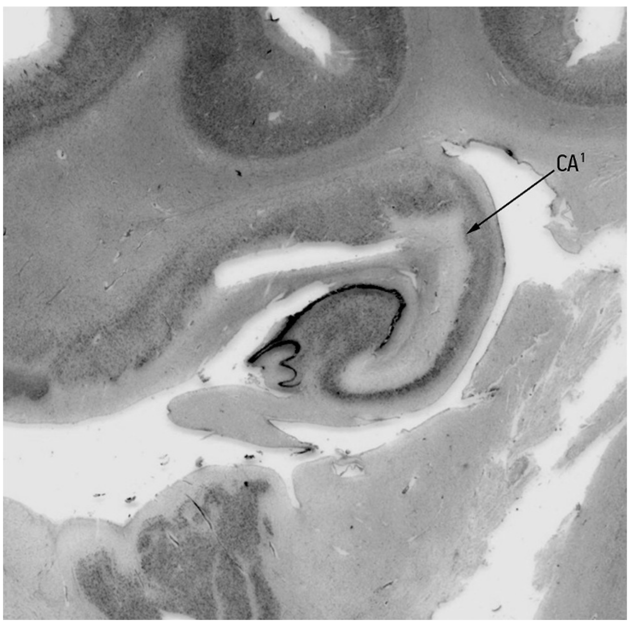

Fig. 1. Male hippocampus (right hemisphere). Stained with cresyl violet, Magnification ×6.

which brains were washed in running water and dehydrated in increasing ethanol concentrations (Table 1).

Frontal sections of thickness 20 μm were cut on a microtome. Some 8000–10000 sections were obtained from each hemisphere. Each 19th, 20th, and 21st (39th, 40th, 41st; 59th, 60th, and 61st, etc.) section (1500 sections) were transferred to a vessel containing water (temperature 34–35°C), where they were floated to flatness; sections were then placed on slides coated with a mixture of protein and glycerol (50:50) and camphor. Slides bearing sections were then transferred to a drying oven at 35–40°C; slides were smoothed and stretched with a brush. Prepared specimens were placed in a drying oven for 25–30 min. Each 40th section (250 per hemisphere) was stained with cresyl violet.

Specimens were examined under a Lecia DM 2500 microscope (Leica, Germany) and field profile areas of pyramidal neurons in the pyramidal layer of field CA1 were measured using ImageScope Color image analysis software (Russian Federation) (objective ×40, ocular ×10). Only those neurons with clearly visible nuclei and nucleoli were measured (n = 100–130). The distribution densities of all glial cells and satellites in the field of view (objective ×40, ocular ×10), in areas of 41500 μm^2, were expressed per mm^2. A total of 10 fields of view in each of the hemispheres studied were examined. The only glial cells counted were those with clear nuclear outlines. Satellite gliocytes were those separated from neurons by distances of up to one gliocyte nucleus diameter.

Statistically significant differences in mean values were identified using Student's t test. The critical significance level was $p < 0.05$.

Results. Cytoarchitectonic and morphometric studies of hippocampal field CA1 in men showed that the structure of the pyramidal layer differed in the right and left hemispheres of the brain (Fig. 1).

Field profile areas of pyramidal neurons in hippocampal field CA1 in the left and right hemispheres were different. The value was greater in the right hemisphere than the left (156.6 ± 2.1 and 149.1 ± 1.9 μm^2, respectively (Fig. 2).

Studies of pyramidal neurons in the pyramidal layer of hippocampal field CA1 in men revealed a tendency to a lower distribution density in the right hemisphere than the left. Thus, the density of pyramidal neurons in field CA1 in the right hemisphere was 575 ± 19 per mm^2, while that in thleft hemisphere was 657.2 ± 38.1 per mm^2 (Fig. 3). Glial cells play an important role in forming the cognitive activity of the human brain [2, 7].

Morphometric studies of the glia in hippocampal field CA1 in the left and right hemispheres of male brains also showed gender-related differences in glioarchitectonics. Thus, the total number of glial cells in field CA1 in the right hemisphere was typically greater than that in the cognate field of the left hemisphere. The distribution density of glial cells in field CA1 in the right hemisphere was 973 ± 18 per mm^2, compared with only 887 ± 11 per mm^2 in the left.

A similar pattern was seen in assessment of satellite glial cells in field CA1 in the left and right hemispheres of the brain. Thus, the proportion of satellite gliocytes among the total number of glial cells in field CA1 reached 63.7 ± 2.0% in the right hemisphere, compared with only 51.6 ± 1.4% in the left.

Discussion. The present study demonstrated the features of the cytoarchitectonic organization of hippocampal field CA1 in the male brain and interhemisphere asymmetry of the cytoarchitectonics of field CA1. This was apparent primarily in the details of the structure of the pyramidal layer of hippocampal field CA1, with right-hemisphere asymmetry of hippocampal field CA1 in the male brain. The literature contains reports of right-hemisphere asymmetry in hippocampal volume. Hippocampal volume in the right hemi-

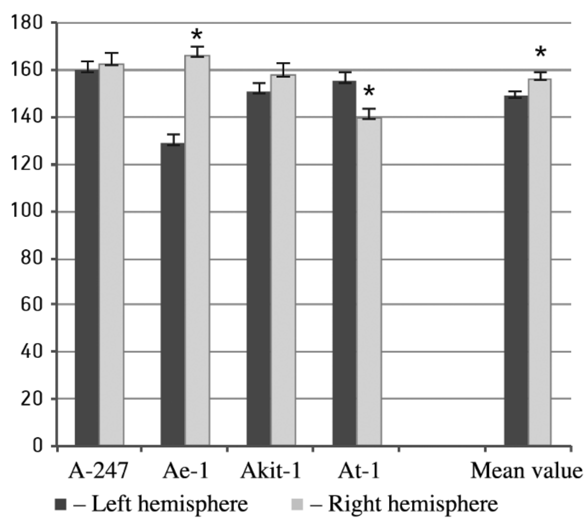

Fig. 2. Neuron field profile areas in the pyramidal layer of hippocampal field CA1 in the male brain. The horizontal axis shows brain ID; the ordinate shows areas, μm^2. Vertical bars show standard errors; *differences between hemispheres significant at $p < 0.05$.

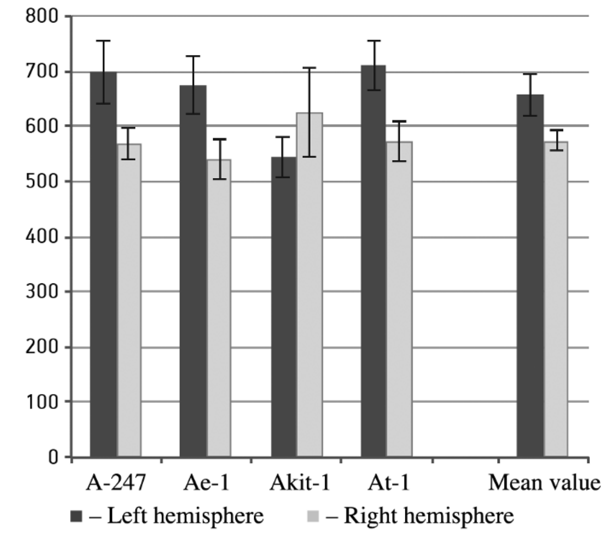

Fig. 3. Neuron density in the pyramidal layer of hippocampal field CA1 in the male brain. The horizontal axis shows brain ID; the ordinate sows the number of neurons per mm^2. Vertical bars show standard errors.

sphere was significantly greater than that in the left [17, 19, 20, 22, 26]. We obtained data showing the presence of larger pyramidal neurons in the pyramidal layer of field CA1 in the right hemisphere. A series of studies [21] also showed different numbers of large neurons in hippocampal field CA1 in the right and left hemispheres. It can be suggested that field CA1 of the right hemisphere has a greater number of connections with other brain formations because of the presence of larger neurons in the pyramidal layer, as the axons of field CA1 neurons are directed to the subiculum and entorhinal cortex and give rise to long collaterals throughout its length.

This study identified interhemisphere asymmetry in neuron distribution density in pyramidal layer of hippocampal field CA1 in men.

These data may correlate with the characteristics of the dendritic structure of pyramidal neurons in the left and right hemispheres of the brain. Data from several studies [14] indicate that the apical dendrite of pyramidal cells divides into a large number of branches, especially close to the point at which they arise from the cell body, forming numerous connections with other cells. Data reported by Sa et al. [18] show that the dendrites of field CA1 pyramidal neurons in different hemispheres of the brain have different structures. The mean length of the terminal segments of apical dendrites of pyramidal neurons in field CA1 was significantly greater in the right hemisphere than the left, which may be one of the causes of the lower concentration of neuron bodies in this area. These points evidently determine the characteristics of the neuron and fiber structure of hippocampal field CA1 in the left and right hemispheres of the male brain and this is associated with the formation of a larger number of connections in field CA1 in the right hemisphere than the left.

We found greater densities of both total glial cells and satellite glial cells in field CA1 in the right hemisphere than the left, which is one of the morphological signs pointing to greater activity in the right hemisphere in males. Neurons in field CA1 are known to be involved in processing recall, the storage of new impressions and events, and the assimilation of new skills [6]. There are studies showing that various cytoarchitectonic formations in the right hemisphere in the male brain have a greater level of involvement in the performance of various tasks associated with working memory, as well as in tasks involving virtual rotation of objects [21]. Clinical, psychological, and physiological studies have drawn attention to the fact that men have better visuospatial memory [12, 13, 23]. Men have good topographic memory and are better at remembering routes and the locations of objects; experimental studies have demonstrated that men find the way out of mazes more quickly than women [24]. Scanning of the brain has shown that London taxi drivers have changes in hippocampal volume depending on taxi-driving experience and knowledge of the city [5]. These data provide evidence of the ability of the brain and particularly the hippocampus to undergo reprogramming and that human activity influences the structural activity of the hippocampus.

It can be suggested that these structural principles of the structure of hippocampal field CA1 in men are associated with the features of cognitive activity in men, their spatial memory, and their ability to both recall and remember events and new skills in work-related activity.

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The authors have no conflicts of interests.

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