Asymmetries in numerical density of pyramidal neurons in the fifth layer of the human posterior parietal cortex

Asimetrije numeričke gustine piramidnih neurona petog sloja zadnje parijetalne kore čoveka

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Abstract

Background/Aim. Both superior parietal lobe (SPL) of dorsolateral hemispheric surface and precuneus (PEC) of medial surface are the parts of posterior parietal cortex. The aim of this study was to determine the numerical density (NV) of pyramidal neurons in the layer V of SPL and PEC and their potential differences. Methods. From 20 (40 hemispheres) formaline fixed human brains (both sexes; 27–65 years) tissue blocks from SPL and PEC from the left and right hemisphere were used. According to their size the brains were divided into two groups, the group I with the larger left (15 brains) and the group II with the larger right hemisphere (5 brains). Serial Nissl sections (5 μm) of the left and right SPL and PEC were used for stereological estimation of NV of the layer V pyramidal neurons. Results. NV of pyramidal neurons in the layer V in the left SPL of brains with larger left hemispheres was significantly higher than in the left SPL of brains with larger right hemisphere. Comparing sides in brains with larger left hemisphere, the left SPL had higher NV than the right one, and then the left PEC, and the right SPL had significantly higher NV than the right PEC. Comparing sides in brains with the larger right hemisphere, the left SPL had significantly higher NV than left PEC, but the right SPL had significantly higher NV than left SPL and the right PEC. Conclusion. Generally, there is an inverse relationship of NV between the medial and lateral areas of the human posterior parietal cortex. The obtained values were different between the brains with larger left and right hemispheres, as well as between the SPL and PEC. In all the comparisons the left SPL had the highest values of NV of pyramidal neurons in the layer V (4771.80 mm⁻³), except in brains with the larger right hemisphere.

Key words: parietal lobe; cerebral cortex; pyramidal tracts; humans; anatomy.

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Introduction

Since Rasdolsky1 relationships between morphological and functional brain asymmetries have been confirmed by numerous investigators for various brain regions2–4. The parietal association cortex of primates comprises areas (Brodmann’s area – BA) BA5 and BA7, also BA39 and 40. The area of the superior parietal lobule (SPL) contains BA5 and 7, which are marked as the area parietalis superior s. medialis5. Anatomically, both SPL of dorsolateral hemispheric surface and precuneus (PEC) of medial surface, are the portions of the same posterior parietal cortical cortex (BA7), which comprises the greatest part of the parietal lobe behind BA2 on medial surface. By far the greatest part of human SPL belongs to BA7, but its detailed parcellation revealed 6 or 8 areas6,7 and several of them had a significantly higher variability in the left hemisphere and/or in men, and for some there was a hemisphere-by-gender interaction7. The cortex of PEC belongs to the medial part of BA7, but is not clearly defined by all authors as posterior parietal cortex8. SPL is a sensorimotor interface for visually guided movements9, and the damage of BA7 leads to different complex types of agnosia10.

This isocortical area has predominant six layered cortex of parietal type, with cinguloparietal transitional zone (BA31) from PEC to suprasplenial part of cingulate gyrus11,12. In studies on the overall cortical connectivity and cortical networks the PEC and posterior cingulate gyrus were consistently observed as centrally connected regions, independent on age and sex13. Within the default brain network one of two prominent areas is the posterior midline region, which includes the posterior parietal cortex (roughly BA31/30/29) and PEC (roughly medial BA7). Their activity associated with impaired visuospatial functioning14. It is specific in recall of episodic memory15, and also with unsuccessful episodic encoding14. The role of PEC in the visual strategy of memory16. In early onset of Alzheimer disease, PEC and hippocampal atrophy are independent from each other and smaller PEC is a support for the stored brains on the bottom of the vessel. Brain tissue fixation period was about four weeks, and after this period we started this study.

After SPL and PEC identification, we measured their extrasulcal surfaces and fronto-occipital distance between the most prominent points of frontal and occipital lobes on each hemisphere, using a line parallel to intercommissural line20. A larger hemisphere was determined according to overlapping of two parameters: longer fronto-occipital distance and larger total (sum) surface of SPL plus PEC. If both of these parameters were larger in one hemisphere, that hemisphere was considered larger. For morphometric analysis in the first group (controls) we included 15 brains with the larger left hemisphere and in the second one five brains with the larger right hemisphere21.

The tissue blocks (0.5×0.5 cm) removed from the middle of SPL and PEC, at equal (1 cm) distance from the hemispheric border in medial (PEC) and lateral direction (SPL), and at the midpoint between the parietoccipital and postcentral sulcus. After paraffin embedding, serial sections (5 μm thick) were stained by Cresyl violet (Nissl method) and used for stereology.

Stereology. For estimation of the density (number) of pyramidal neurons in the layer V of SPL and of PEC the relative stereological parameter, Nv, was applied22,23.

The numerical density was determined on 5 μm thick sections stained by Cresyl violet, under magnification 40×, when a grid was inserted into the ocular of microscope (test system) M42 (Weibel), which was adjusted for the given magnification by an objective micrometer. The test system and microscope were calibrated by an objective micrometer 1:100 at the used magnification (ocular magnification 10× and objective 40×), and the determined surface area (At) of the test system was 0.058 mm2. The formula of Floderus22 was used for the numerical density:

$N_V = \frac{N_A}{(t + D - 2h)}$, where $N_V$ is the numerical density of pyramidal neurons, N/A the number of pyramidal neurons on the test system surface, t is the thickness of a section (5 μm), D an average diameter of pyramidal cell (0.033 mm) and h is the constant (height of lost cap). This constant h is calculated according to the formula:

$h = R - \left( R^2 - r^2 \right)^{1/2}$,

where R is the maximal measured diameter (0.066 mm), and r the minimal measured diameter (0.0055 mm) of a pyramidal neuron. The average diameter of a neuron was determined by an objective micrometer 1:100 at the used magnification (ocular 10× and objective 40×) on 100 randomly selected pyramidal neurons of the fifth layer.

Pyramidal neurons counting was performed in 10 fields sampled in standardized way, from the cortical surface to

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by moving the test system vertically down from the cortical surface to this layer. After returning to the surface, the test system was moved horizontally for one field and movement was repeated down to the same layer. The final values were obtained as middle values of these measurements.

In descriptive and analytical statistics (significance of differences by t-test, SD, SE) software “InStat 2” was used. We analyzed separately NV in SPL and PEC in brains with the larger left and in brains with the larger right hemispheres and compared the investigated structures on the left and right sides of these brains.

Results

The obtained values for NV of pyramidal neurons of the layer V in SPL and PEC are shown in the Table 1 with significant differences marked by letters a-h.

We found a significantly higher numerical density in the left SPL in the larger left hemispheres than in left SPL in larger right hemispheres, without other significant differences between the brains with larger left and right hemispheres.

In brains with the larger left hemisphere the left SPL had a significantly higher NV than the right one, the left SPL had a significantly higher NV than the left PEC, and the right SPL had significantly higher NV than the right PEC.

In brains with larger right hemispheres the left SPL had significantly greater NV than the left PEC, the right SPL had larger density than the left SPL, right PEC had higher density of neurons than the left one, and the right SPL had higher NV than the right PEC.

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The left hemisphere is dominant for language, and the right one for visuo-spatial orientation, and the larger dimensions of the left hemisphere include its larger cortical surface (left 840.0 cm², right 838.0 cm²). Much more frequent findings of larger left hemisphere and of longer left Sylvian fissure are related to the great majority of right-handers in population, and to left hemisphere dominance, including the localisation of speech centers in left hemisphere. We did not know the data about hemisphere dominance of the investigated brains, but according to detailed analysis of the literature and available morphological studies, our hypothesis that larger hemispheres were those with both, a longer fronto-occipital distance (brain length), and the sur-

### Table 1

| SPL/PEC | NV (nm⁻³), X ± SD (min-max) |
|---------|----------------------------|
|         | right hemisphere | left hemisphere |
| SPL     |                 |                 |
| left    | 3954.2 ± 187.5  | 4771.8 ± 169.6  |
|         | (3583–4089)     | (4510–4932)     |
| right   | 4478.4 ± 59.3   | 4257.4–145.9    |
|         | (4393–4553)     | (4089–4468)     |
| PEC     |                 |                 |
| left    | 3464.4 ± 330.2  | 3852.6 ± 43.1   |
|         | (2993–3759)     | (3793–3920)     |
| right   | 4013 ± 162.9    | 3675.1 ± 81.8   |
|         | (3794–4218)     | (3541–3794)     |

*a p < 0.01 vs left SPL in the right hemisphere
* p < 0.01 vs right SPL in the left hemisphere
* p < 0.01 vs left PEC in the left hemisphere
* p < 0.01 vs right PEC in the left hemisphere
* p < 0.05 vs left PEC in the left hemisphere
* p < 0.01 vs left SPL in the right hemisphere
* p < 0.01 vs left PEC in the right hemisphere
* p < 0.01 vs right PEC in the right hemisphere

Our finding of greater NV in the left SPL only in brains with the larger left hemisphere is in agreement with the majority of recent studies, which unfortunately did not consider the hemispheric dominance. So, between the two hemispheres there are globally and regionally specific differences, with the generally thicker cortex and with a larger number of neurons in the left hemisphere in both sexes. A significant leftward asymmetry was found in the precentral gyrus, middle frontal, anterior temporal and SPL, and under the condition of unconditioned love compared with the control condition the left SPL (BA7) was most significantly activated.

However, our results could be in discordance with the findings of significant rightward asymmetries of posterior brain regions on the medial surface, and that one of two hemispheric asymmetries for spatial attention control was a region in only right, but not left SPL. Areas specifically
implicated in generating and playing scales (music) were posterior cingulate, middle temporal, right middle frontal, and right PEC cortices, what can be related to our finding of larger right PEC only in brains with larger right hemispheres. PEC is involved in the network of the neural correlates of self-consciousness, engaged in self-related mental representations during rest and the most significant restoration of glucose metabolism (recovery of consciousness after severe chronic brain damage) occurs in cortices of PEC and cuneus.

The representative parietal cytoarchitecture of human BA7 is characterized by fully differentiated isocortex: a columnar pattern with conspicuous layers II, IV, V and VI. Radial neuronal arrangement, horizontal dendritic branching and greater similarity to the majority of pyramidal (non-Betz) neurons are clear characteristics of BA7 large pyramidal neurons of lamina V. The presence of several basal dendrites corresponds better to the majority of pyramidal (non–Betz) cells. Horizontal orientation of both basal and apical dendritic branching fits well with the hypothesis about the role of lamina V pyramidal neurons in intracortical selection of impulses which would leave cortex and indicate their role in associative processing. In BA7 both stripes of Baillarger are visible indicating a considerable presence of horizontal axons, probably of long-range connections. Therefore, regional differences in Nv of the layer V pyramidal neurons that we found are consistent with the existence of different subsets within the brain default mode networks (long-range neuronal pathways), with the pivotal role of PEC/posterior cingulate cortex. Additionally, findings that pyramidal neurons of the layer V of the adult rodent cortex fall into two major classes, type I cells and type II, lead to the question if their different distributions in parietal cortex cause the differences in the values of Nv.

In our previous study in brains with larger left hemisphere, the cortex of the left SPL was significantly thicker as compared to the left PEC, without other significant differences, what related to our present results further multiplies the number of neurons in the left SPL. In brains with the larger right hemisphere the cortex of SPL was bilaterally thicker than of PEC. The lower Nv in the cortex of PEC we found, shows the more loose arrangement of neurons. Asymmetries in terms of cortical thickness reported for SPL (left > right) and PEC (right > left) with more pronounced differences in men, and findings of higher amounts of parietal gray matter in the left hemispheres, are in agreement with our results for brains with larger left hemispheres. In general, our results confirm the statement that differential parietal macroanatomy between genders and hemispheres still is a matter of debate. In addition to the provided numerical data, our results lead to increasing complexity of knowledge about the relationships between morphological asymmetry and the function of human cortex.

Conclusion

Morphometric studies of human brain should unavoidably include the data about lateralization (handedness), cerebral dominance, or at least, about larger hemisphere.

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