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MINICOLUMNAR STRUCTURE IN HESCHL'S GYRUS AND PLANUM TEMPORALE: ASYMMETRIES IN RELATION TO SEX AND CALLOSAL FIBER NUMBER

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Abstract—Aim: To investigate the cytoarchitectural basis of asymmetries in human auditory cortex. Minicolumn spacing and number, and regional cortical volume and surface area were measured in the primary auditory region (Heschl's gyrus, HG) and posterior auditory association region (planum temporale, PT) in 17 neurologically normal adults (10 female, seven male). PT surface area, minicolumn spacing and minicolumn number were greater in the left hemisphere. HG surface area was larger in the left hemisphere. Asymmetries of minicolumn number in primary and association auditory regions correlated with axonal fiber numbers in the subregions of the corpus callosum through which they project. PT minicolumn number was more asymmetrical in men than women but total number was similar in the two sexes. We conclude that asymmetry of the surface area of the PT is a function of minicolumn spacing. Fewer callosal projections between the plana are found when the minicolumn spacing is more asymmetrical. © 2006 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: auditory cortex, corpus callosum, language, sex difference, minicolumn, association cortex.

The planum temporale (PT), comprising unimodal auditory association cortex, posterior to the primary auditory cortex in the superior temporal gyrus (STG), has a greater size on the left (Geschwind and Levitsky, 1968; Harasty et al., 2003). It has been proposed that the hemisphere in which a given brain area is larger is dominant for the associated function (Galaburda, 1995). The left hemisphere is usually dominant for speech processing in humans. What is the cellular basis of this asymmetry and how does it relate to the main path for inter-hemispheric transmission, the corpus callosum?

During embryonic development, the cells of the brain migrate toward the surface, forming minicolumns in the cortex. These are grouped into larger macrocolumns to form the basis of the mapping of functions across the brain's surface. The radial unit hypothesis (Rakic, 1995) proposes that proliferation of radial minicolumnar units of cells underlies the expansion of different cortical surface regions during development and across species.

Auditory cortex in the STG develops a clear columnar cell distribution by the third trimester of fetal life, which is established in early childhood, although axonal maturation continues up to at least 12 years of age (Moore and Guan, 2001). Radial organization of physiological response properties indicates functional macrocolumnar organization in primary auditory cortex with topological mapping of stimulus features such as frequency and ear preference (Linden and Schreiner, 2003). Examination of minicolumnar structure bridges the gap between cortical fine structure and functional asymmetry. Cytoarchitectural columns have electrophysiological counterparts, identified by single unit recordings, in which cells within a column share similar stimulus sensitivity. The combination of stimulus sensitive columns in a region presumably confers processing specialization contributing to functional asymmetry.

The left hemisphere is dominant at processing speech due, in part, to an ability at processing shorter temporal transitions in the speech signal (Efron, 1963; Tallal et al., 1993; Zatorre et al., 2002; Shtyrov et al., 2000). Furthermore, in the interpretation of word meaning the left hemisphere activates narrow semantic fields, whereas, the right hemisphere activates wide semantic fields appropriate to its greater sensitivity to context (Rodel et al., 1992). Anatomically, these asymmetries may be facilitated by asymmetry in columnar organization. Macrocolumns are more widely spaced in the left than in the right auditory association cortex (Galuske et al., 2000). Minicolumns are more widely spaced in the PT of the left hemisphere, an asymmetry that is absent in non-human primate brains (Buxhoeveden et al., 2001). Witelson et al. (1995) found that women have a greater density of neurons in posterior PT, which they interpreted as a sex difference in input to cortical columns.

The goal of the present study was to examine minicolumn asymmetry in Heschl's gyrus (HG) and the PT in men and women, and relate it to cortical surface size and axonal distribution in the corpus callosum of the same subjects. The association of minicolumnar organization with callosal connectivity, and sex differences in minicolumns have not been investigated previously. We predicted that area PT would be more asymmetrical than HG, men would be more asymmetrical than women, and that minicolumn number asymmetry would correlate with callosal axon number.

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Abbreviations: HG, Heschl's gyrus; PT, planum temporale; rmANOVA, repeated measures analysis of variance; STG, superior temporal gyrus.

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Table 1. Demographic details of the brain collection (mean and standard deviation)

Sex	Age (y)	Postmortem interval (mo)[a]	Fixation time (mo)	Total brain weight (g)[b]
Male (*n*=7)	59.9±11.9	36.4±15.9	20.9±9.8	1102.5±91.3
Female (*n*=10)	73.2±12.4	36.9±19.0	26.9±13.3	962.2±99.8

Handedness data were not available for these deceased subjects.

[a] Accurate information not available for one case.

[b] Accurate information not available for two cases.

EXPERIMENTAL PROCEDURES

Tissue and demographics

Formalin-fixed brain tissue was sampled from 17 neurologically normal adults who had died between the ages of 40 and 90 years (10 female, seven male). Tissue was collected with consent in accordance with standard neuropathological practice and is registered with UK national investigations on organ retention. All cases are catalogued and none has been recalled. Cases were selected to yield comparable group mean fixation times and ages at death as far as possible, although pair matching was not possible. Patients were included on the basis of the assessment of clinical notes by a consultant psychiatrist (T. J. Crow or Dr. S. J. Cooper, Regional Neuropathology Laboratory, Royal Hospitals Trust, Belfast, UK). Pathological assessment of tissue samples was carried out by a consultant neuropathologist (M. M. Esiri or B. McDonald, Oxford) and cases with significant pathology, such as Alzheimer's disease, were excluded using CERAD criteria. Demographic details and potentially confounding variables, including age at death, postmortem interval, and fixation time, were subjected to statistical analysis (see Table 1).

Tissue processing

During dissection, HG and the PT situated in the Sylvian fissure, on the superior surface of the temporal lobe, were painted to aid identification; 5 mm thick blocks of temporal lobe were cut orthogonal to the long axis of the lobe, systematically random with respect to the anterior boundary of HG. ("Systematically random" is a standard stereological term referring to systematic (regular) sampling of a structure starting at a random position within the first sampling unit in order to minimize sampling bias.) All blocks were used for the assessment of gross measurements. For the analysis of minicolumns, after the blocks were embedded in paraffin wax, two 25 μm thick sections were cut from each region of interest of each hemisphere by systematically random sampling from the blocks. A Cresyl Violet Nissl stain was used for the measurement of minicolumn parameters. Each region of interest was analyzed on two slides in each hemisphere. Tissue shrinkage due to embedding in these brains has been estimated with a mean of 23.7% and no systematic difference was found across subjects.

Gross anatomical measurements

HG was defined as HG, bounded by Heschl's sulcus posteriorly, the first transverse sulcus anteriorly (Kim et al., 2000) and laterally by the superolateral margin of the STG (Zetzsche et al., 2001) containing cytoarchitectural regions TC and TBC following the definitions of Von Economo and Koskinas (1925). The lower bank of the sylvian fissure, posterior to the HG was measured as the PT. This consisted of the PT bounded anteriorly by Heschl's sulcus, including regions TB and TA1, excluding the posterior ascending ramus.

For this postmortem tissue the PT was painted while still intact to clearly identify the beginning of the ascending ramus as the posterior border of the PT. This has an advantage over the single "knife-cut" method (following Larsen et al., 1989) which is vulnerable to variation in the beginning of the ascending ramus depending on where on its medial–lateral extent the knife-cut is made. The painted boundary excludes this error in the asymmetry measure but it remains that several authors have found that the more anterior ascending ramus of the right hemisphere leads to a shorter measure of the horizontal PT on the right. It is unclear whether or not the ascent of the posterior sylvian fissure marks a meaningful transition in cortical structure or function. The posterior PT is part of parietal cortex and may be more functionally correlated with the functions of the parietal lobe than with speech functions (Zetzsche et al., 2001). Since minicolumn spacing is not homogenous in the cortex (Chance et al., 2006), the evidence that the cytoarchitecture of the posterior sylvian fissure has a transitional structure between temporal and parietal cortex (Braak, 1978) provided the most compelling argument to confine the present investigation to the temporal cortex of the horizontal PT.

Callosal subregions were defined as proportions of the total length of the corpus callosum with reference to the anatomical landmarks of the genu and splenium, as reported in Highley et al. (1999), similar to the system of Aboitiz et al. (1992a,b), and Witelson (1989). The midbody constituted the middle third of the callosal length and the isthmus consisted of the posterior third excluding the splenium (see Highley et al., 1999 for further details).

Surface areas were measured using stereological probes on photographed coronal slices, every 5 mm throughout the temporal lobe, prior to the selection of a subset for minicolumn analysis. Photographed images were projected on to a screen for measurement. Cortical volume was estimated by unbiased, scaled point counting within the grey matter of each region. Surface area was estimated by counting intersections between the cortical surface and cycloidal test lines of known dimensions. A parallel slice design was used as reported by Pakkenberg and Gundersen (1997). Each structure was sampled twice to generate a mean estimate. Estimation of PT and HG surface area and cortical volume was repeated for 10 hemispheres to determine reliability. The intraclass correlation coefficient was equal to or in excess of 0.9 for each of the four measures, indicating reliable measurement.

Columnar measurements

Minicolumn spacing was quantified using an automated and unbiased image analysis program (Fig. 1). The method has been reported in detail by Buxhoeveden et al. (2001). Minicolumns are clearest in lamina III, so minicolumn detection was optimized for lamina III. In summary, lamina III was photographed at 100× magnification, normal to the cortical surface, and the photomicrographs were digitized at 0.48 μm resolution and tessellated. Two micrographs were generated from each slide, each micrograph comprising a region approximately 1.5 mm^2 in area. Fields were selected randomly excluding the fundi of sulci or the apices of gyri (regions of high cortical curvature).

The image was automatically segmented to select neurons and nearest neighbor measurements of clustering were applied to determine the periodicity of columnar distribution. Segmentation was based on grey level intensity of the digitized image, with