Sex Differences in the Inferior Parietal Lobule

The inferior parietal lobule (IPL) – a neocortical region and part of the heteromodal association cortex (HASC) – has been hypothesized to exhibit sexual dimorphism, as do other HASC regions, particularly with regard to asymmetry. Using a reliable method for measuring IPL gray matter volume based on individual sulcal–gyral landmarks, we measured this region on magnetic resonance imaging scans from a sample of 15 individually matched pairs of normal male and female subjects. Male subjects showed significantly larger left, but not right, IPL volumes when compared to females. Males also showed a leftward (left > right) asymmetry for the IPL, with a less marked opposite asymmetry in females. Such sexual dimorphisms may possibly underlie the subtle cognitive differences observed between the sexes.

Introduction

The inferior parietal lobule (IPL), a neocortical region, also referred to as the posterior parietal cortex (Mesulam, 1998), consists of the supramarginal gyrus, an arched lobule surrounding the end of the lateral fissure, and the angular gyrus, a lobule surrounding the parallel sulcus’ ascending posterior segment (Fig. 1) (Duvernoy, 1991). It corresponds, in part, to Brodmann areas 39 and 40 (Brodmann, 1909), and is part of the heteromodal association cortex (HASC), which also includes the planum temporale (PT), the dorsolateral prefrontal cortex (DLPFC) and the inferior prefrontal area (Broca’s area) (Mesulam, 1985, 1998). Previously, HASC regions, in conjunction with other cortical areas, were believed to serve as sites of higher-order multimodal convergence integrating all aspects of mental function (Mesulam, 1985, 1998). More recently, however, this view has been modified in that these regions not only have interconnections with one another, but also reciprocal connections with lower-order unimodal areas (Mesulam, 1998). According to Mesulam, these regions serve as ‘epicentres for a large-scale network’ with each epicentre ‘potentially belonging to several intersecting networks’ (Mesulam, 1998). Similarly, the IPL has been noted to have a role in processing information from the visual, auditory and somatosensory association cortices (Geschwind, 1964), as well as having connections with other HASC regions, the limbic system and the hypothalamus (Zec and Weinberger, 1986).

The IPL, like other HASC regions, is among the latest both to evolve and to develop, based on phylogenetic and myelogenetic evidence (Geschwind, 1964; Mesulam and Geschwind, 1978). These regions have often been noted on magnetic resonance imaging (MRI) or neuropathology to be usually highly lateraled, with the region in one hemisphere having greater area or volume compared to the other (Geschwind and Levitsky, 1968; Galaburda et al., 1978; Eidelberg and Galaburda, 1984; Foundas et al., 1995, 1998; Pearson et al., 1996; Raz et al., 1997; Honeycutt and Frederikse, 1999). For example, in a neuro-anatomical study, Eidelberg and Galaburda found leftward asymmetry in the angular gyrus (Eidelberg and Galaburda, 1984). These regions also exhibit normal sex differences, especially with regard to asymmetry (Geschwind and Galaburda, 1985; Gur et al., 1991; Witelson and Kigar, 1992; Kulynych et al., 1994; Barta et al., 1995; Marsh and Casper, 1998; Honeycutt and Frederikse, 1999) and relative volume (Schlaepfer et al., 1995; Harasty et al., 1997; Kennedy et al., 1998). Such sexual dimorphisms may underlie some of the normally observed subtle but significant cognitive differences between the sexes (Maccoby and Jacklin, 1974). For example, men tend to perform better on visuospatial tasks, whereas women generally have greater verbal abilities (Bakan and Putnam, 1974; Benbow and Stanley, 1980; Gladue et al., 1990; Holdien, 1991).

The parietal lobes subserve cognitive functions primarily involving attention and perception. More specifically, the IPL is involved in selective attention (Petersen et al., 1989; Mirsky et al., 1992; Heilman et al., 1993) and visuospatial processing (Keating and Gooley, 1988; Petersen et al., 1989). Some of these cognitive tasks appear to lateralize to either the right or the left parietal lobe. For example, the right parietal lobe may be more involved in spatial working memory tasks (Jonides et al., 1993), sensory relationships between body parts (Cutting, 1991) and the recognition of affect (Borod et al., 1986; Cleghorn et al., 1989a,b). The left IPL is more involved in cognitive tasks related to perception, such as mental rotation of three-dimensional figures (Alivisatos and Petrides, 1997), judgments of target speed (Corbetta et al., 1991) and position (Lacquaniti et al., 1997), time estimation (Maquet et al., 1996), complex motor planning (Winstein et al., 1997) and non-semantic aspects of verbal processing (Vandenberghe et al., 1996).

Thus, given normal sex differences in brain structure and function, especially with regard to asymmetries in HASC regions, and normal lateralization of cognitive functions, it is reasonable to hypothesize that sex differences in structural IPL asymmetry may underlie some sex differences in cognitive functioning. Indeed, in an MRI study of cortical volumes Kennedy et al. found normal sex differences in the parietal lobe, but although left and right hemispheric measurements were obtained, the authors did not specifically examine sex-by-hemisphere interactions (Kennedy et al., 1998). As sex-based asymmetries in the IPL have not previously been examined, we thus made the following hypotheses: (i) males have greater total IPL volumes compared to women, (ii) males have larger left versus right IPL volumes and (iii) males have larger left IPL volumes compared to women.

Materials and Methods

Subjects

We examined 15 pairs of normal male and female subjects who were individually matched on age (±5 years), race, handedness and parental socioeconomic status (Holingshead, 1975), giving a total of 30 subjects.
The male versus female groups did not differ significantly on age (mean age of males = 39.7 years, range = 24–58 years; mean age of females = 38.4 years, range = 23–53 years), race (86.67% Caucasian and 13.33% non-Caucasian in both gender groups) or family socioeconomic status (20% of level 2 and 80% of level 3 in both gender groups). All 30 subjects were right-handed as assessed by the Chapman inventory (Chapman and Chapman, 1987).

Volunteer study subjects were recruited from the community via advertisement (n = 12), via random telephone-digit dialing as part of a community-based aging study (n = 4), as well as from the Epidemiologic Catchment Area (ECA) study (Regier et al., 1984) (n = 5). In addition, nine subjects served as normal controls in a study by a collaborator in London. No subjects had a history or MRI evidence of overt brain disease (via radiological interpretation), lifetime history of substance abuse/dependence or any medical illnesses known to affect the brain, e.g. severe head injury with loss of consciousness >1 h, severe hypertension (e.g. requiring treatment with two or more medications), or significant cardiovascular disease requiring medical or surgical treatment. In addition, subjects had no current or history of major mental illness as assessed by the Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990) and DSM III-R criteria, or in any first-degree relatives (assessed by questionnaire).

**Magnetic Resonance Imaging**

All subjects gave written informed consent in accordance with institutional standards. MRI scans were obtained on one of three GE Signa 1.5 T units all using the same edition of GE software and identical scanning sequences. Approximately equal numbers of male and female subjects were scanned on each MRI unit. Contiguous slices were acquired through the entire brain in the coronal plane using a spoiled gradient recall acquisition in the steady state (GRASS) sequence (TE = 35, TR = 5) with a flip angle of 45°. Slices were 1.5 mm thick with a field of view of 20 or 24 and a matrix size of 256 × 256.

**Image Processing and Measurement**

All raters were blind to subject sex. Using the software ‘Measure’ developed in our laboratory (Barta et al., 1997), raters stripped all brains of skull and dura via reliable semi-automated techniques (Ayward et al., 1997; Buchanan et al., 1998). Realistic three-dimensional brain images were rendered, enabling easy visualization of sulcal-gyral patterns. All brains were aligned along the anterior-posterior commissural (AC-PC) line and the interhemispheric fissure.

By using a ‘paint and point-counting’ method similar to that described by Buchanan et al. for subparcellating the frontal lobe (Buchanan et al., 1998), the IPL was first delineated by painting along the IPL sulcal-gyral landmarks on a cortical surface three-dimensional rendering. These painted boundaries would later (see below) be superimposed upon two-dimensional orthogonal slices in order to select grid points lying within the boundaries. Utilizing such surface renderings for determining sulcal-gyral landmarks and transferring these boundaries to serial sections has been described by other authors (Damasio and Frank, 1992; Barta et al., 1995; Kulynych et al., 1996). For a more in-depth discussion of these techniques, as well as a detailed description of our IPL measurement methodology, see M.E. Frederikse et al. (submitted). The IPL boundaries included the postcentral sulcus anteriorly and the intraparietal sulcus superiorly. The inferior boundary consisted of: (i) the Sylvian fissure from the postcentral sulcus to the planum temporale (PT) posterior lateral edge; (ii) a plane passing through the PT posterior lateral edge and the temporo-occipital incisure to the superior temporal (or parallel) sulcus; and (iii) the parallel sulcus to its horizontal segment (anterior occipital sulcus) and its connection with the intraparietal sulcus.

The SPGR data set was filtered using locally developed anisotropic diffusion filtering software (K = 1.5 × average sigma value of ten random values within the caudate nucleus; number of iterations = 3) to better visualize the gray-white boundary (Gerig et al., 1990). A three-dimensional grid of points spaced 4.5 mm apart and yielding ~200 points per IPL was superimposed on the entire volume. ‘Paint’ demarcating the IPL anatomical borders was then superimposed upon the filtered image set, and gray matter points lying within the painted borders were selected. Both this stereological volume estimation method (Cavaliere') (Barta et al., 1997) and the paint method (Buchanan et al., 1998) have been discussed in previous publications. Due to imprecise white matter

Figure 1. Surface (three-dimensional) view of brain (reconstructed from MR images) with inferior parietal lobule (IPL) highlighted. The supramarginal and angular gyri are labeled.
boundaries for this and other cortical regions, IPL white matter volumes were not obtained. Interrater reliability for the volume measurement yielded an unbiased intraclass coefficient (of Bartko and Carpenter) of 0.98 in five randomly selected brains.

**Results**

Total brain volume (TBV), calculated from the total stripped brain via voxel tally (Aylward et al., 1998), left IPL gray matter volume and right IPL gray matter volume were calculated using locally developed software (Barta et al., 1997). Total IPL volume was derived from the sum of left and right IPL volume. Table 1 summarizes the mean measurement data.

Using three separate one-way analyses of variance (ANOVA), there was no effect of MRI scanner on TBV ($F = 0.20, df = 2.29, P = 0.82$), left IPL volume ($F = 0.60, df = 2.29, P = 0.56$) or right IPL volume ($F = 0.02, df = 2.29, P = 0.98$).

In order to determine if TBV need be a covariate in the statistical analysis, ANOVA of TBV between males and females was first conducted. This analysis revealed no significant difference in TBV between males and females ($F = 2.63, df = 1.29, P = 0.12$), indicating no need to covary for TBV. Repeated-measures ANOVA was then conducted with hemisphere as the repeated measure and sex as the between-subjects variable. This analysis revealed a main effect of sex ($F = 11.66, df = 1.28, P < 0.01$), with males having significantly larger total IPL volume than females. Although there was no main effect of hemisphere ($F = 2.60, df = 1.28, P = 0.66$), the hemisphere-by-sex interaction approached statistical significance ($F = 3.47, df = 1.28, P = 0.07$).

Given our hypothesis that the left IPL is larger than the right in men, repeated-measures ANOVA was performed in males only with hemisphere as the repeated measure. In this analysis, left IPL volume was not significantly greater than right IPL volume in men ($F = 3.03, df = 1.14, P = 0.10$).

Because of the significant sex difference in total IPL volume, as well as our a priori hypotheses, we wanted to examine which side contributed most to the male/female total IPL volume difference. Analyses of variance revealed that men had significantly larger left IPL volumes compared to females ($F = 11.54, df = 1.29, P = 0.02$). The right IPL, however, showed no significant sex differences on ANOVA ($F = 3.18, df = 1.29, P = 0.09$). Figure 2 depicts mean IPL volume/TBV ratios in the left and right IPLs for males versus females, demonstrating that the left, but not the right, IPL is significantly larger in males compared to females.

**Discussion**

In summary, this study demonstrates that men have larger total IPL volumes when compared to women, with this difference being largely due to greater left male IPL volume. The total brain volumes in this study are in reasonable accordance with those of other studies (Schlaepfer et al., 1995; Aylward et al., 1998; Goldstein et al., 1999) with differences likely due to methodological variability. In addition, the IPL volumes obtained in this study are remarkably similar to those found by other authors (Kennedy et al., 1998) as seen in Table 2. While we measured the IPL region as a whole, as opposed to individual gyri as did Kennedy et al. (Kennedy et al., 1998), our volumes closely approximate the sum of their mean volumes obtained for angular gyrus, anterior and posterior supramarginal gyri, and parietal operculum. These similarities are evident not only for left versus right IPL volumes, but also for males versus females (see Table 2).

This study replicates previous studies in which the IPL showed leftward asymmetry (Eidelberg and Galaburda, 1984; Iwasaki et al., 1986, 1990; Raz et al., 1997). However, this study is the first to identify sex differences with respect to left, but not right, IPL gray matter volume, i.e. that the left IPL is larger in male subjects as compared to females. Furthermore, while our results were not statistically significant, this study also supports data from other studies demonstrating that males tend to have more leftward-lateralized brains than do females (Witelson and Kigar, 1992; Kulynych et al., 1994), with females generally having either no lateralization or a rightward asymmetry [reviewed by Marsh and Casper (Marsh and Casper, 1998)]. It is possible that with a larger sample, the leftward-lateralized male pattern would then be significant.

In a cytoarchitectonic parcellation of the parietal lobes of eight human brains, Eidelberg and Galaburda showed leftward asymmetry for most of the angular gyrus (area ‘PG’), correlating with a larger left planum temporale (Eidelberg and Galaburda, 1984). Conversely, another, yet smaller, portion of the angular gyrus (area ‘PEG’), corresponding to the most posterior-superior aspect of the gyrus, showed rightward asymmetry.
As described previously, men tend to outperform women on tasks of visuospatial processing, a function subserved by the IPL, particularly the left side. Given the finding of larger left IPL volume in males compared to females, this study provides a possible structural brain basis for such sex-based cognitive differences. In addition, this cross-sectional study only attempts to describe male–female structural differences in the IPL, and does not permit making conclusions as to male–female brain developmental differences. Future studies, e.g. functional neuroimaging studies, assessing activation during cognitive tests specific to parietal regions, as well as longitudinal studies, with an emphasis on sex differences, lateralization and development, in normal states would be useful.

Notes
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Several studies have demonstrated global and regional brain sexual structural dimorphisms, in both normal children and adults (Witelsen and Kigar, 1992; Dreisen and Raz, 1995; Schlaepfer et al., 1995; Raz et al., 1995, 1997; Reiss et al., 1996; Giedd et al., 1997; Kennedy et al., 1998). These studies indicate the presence of sex-associated differences in cerebral development and organization, processes most likely beginning during fetal development [reviewed by Marsh and Casper (Marsh and Casper, 1998)]. Of note, Schlaepfer et al., using 5 mm MRI sections and approximations to cortical regions of interest, demonstrated that in addition to women having significantly smaller brains compared to men, regional brain sex differences also existed. However, total IPL gray matter percentages were not significantly different between men and women (Schlaepfer et al., 1995).

While our study was conducted in an exceptionally well-matched sample population and utilized a highly reliable measurement method, the lack of accompanying detailed neuropsychological data makes direct comparison between brain findings and cognitive data speculative. Other possible methodological deficiencies of this study include: (i) lack of IPL white matter measurements, (ii) using right-handed subjects only and (iii) rats not being blind to hemisphere being measured. As there are no precise white matter boundaries for the IPL, as well as other cortical structures, we are unable as yet to develop reliable measurement techniques for the white matter. As for the issue of handedness, many asymmetrical brain measures, e.g. planum temporale and radius of gyration, have correlated with handedness (Steinmetz et al., 1991; Bullmore et al., 1995). Thus, it is possible that left-handed individuals show variants of the pattern we demonstrated. Whereas raters were blind to subject gender, the current imaging software does not allow for techniques such as counterbalanced mirroring which would blind raters to hemisphere, and thus experimenter bias may conceivably be a factor in these measures.

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