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CORTICAL SURFACE AREA AND CORTICAL THICKNESS IN THE PRECUNEUS OF ADULT HUMANS

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Abstract—The precuneus has received considerable attention in the last decade, because of its cognitive functions, its role as a central node of the brain networks, and its involvement in neurodegenerative processes. Paleoneurological studies suggested that form changes in the deep parietal areas represent a major character associated with the origin of the modern human brain morphology. A recent neuroanatomical survey based on shape analysis suggests that the proportions of the precuneus are also a determinant source of overall brain geometrical differences among adult individuals, influencing the brain spatial organization. Here, we evaluate the variation of cortical thickness and cortical surface area of the precuneus in a sample of adult humans, and their relation with geometry and cognition. Precuneal thickness and surface area are not correlated. There is a marked individual variation. The right precuneus is thinner and larger than the left one, but there are relevant fluctuating asymmetries, with only a modest correlation between the hemispheres. Males have a thicker cortex but differences in cortical area are not significant between sexes. The surface area of the precuneus shows a positive allometry with the brain surface area, although the correlation is modest. The dilation/contraction of the precuneus, described as a major factor of variability within adult humans, is associated with absolute increase/decrease of its surface, but not with variation in thickness. Precuneal thickness, precuneal surface area and precuneal morphology are not correlated with psychological factors such as intelligence, working memory, attention control, and processing speed, stressing further possible roles of this area in supporting default mode functions. Beyond gross morphology, the processes underlying the large phenotypic variation of the precuneus must be further investigated through specific cellular analyses, aimed at considering differences in cellular size, density, composition, and structural covariance compared to other brain areas.

Key words: brain morphology, parietal lobes, surface-based morphometry, neuroanatomy.

INTRODUCTION

The precuneus of the human brain has received much attention in the last decade (Margulies et al., 2009; Zhang and Li, 2012). For long time parietal areas have been somehow neglected in terms of comparative neuroanatomy and functional analyses, at least when compared with other cortical districts that have received more consideration through the history of neuroscience. Generally, studies have been devoted to non-human primates more than to human brain, probably because of the difficulties associated with investigating deeper cortical volumes (see Mountcastle, 1995). The precuneus is involved in integration between visuo-spatial inputs and memory, bridging somatosensory and visual cortex, and directly fading into posterior cingulate and retrosplenial areas (Cavanna and Trimble, 2006). It is a major node of main functional and structural networks of the human brain (Hagmann et al., 2008), with a relevant role within the Default Mode Network (Buckner et al., 2008; Utevsky et al., 2014). Recently, the precuneus has been shown to be also involved in the early stages of Alzheimer's disease, further evidencing the importance of these areas in processes associated with energetic and physiological balance of the human brain (Jacobs et al., 2012; Doré et al., 2013; Huang et al., 2013). The parietal elements are even more interesting considering that spatial changes associated with their size and proportions characterize the geometry of the brain in *Homo sapiens* when compared with the brain form of extinct human species (Bruner et al., 2003, 2011a; Bruner, 2004, 2010).

A recent analysis of the midsagittal morphology showed that the proportions of the precuneus are a major source of brain shape variation among adult humans (Bruner et al., 2014a). The longitudinal extension of this area generates the largest differences among individuals, and it influences the overall form of the brain. The spatial changes associated with intra-specific variation of the precuneus is strongly related to spatial changes associated with cranial differences between modern and non-modern human species, suggesting that the origin of the

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Abbreviations: ANOVA, analysis of variance; CSA, cortical surface area; DAT, Differential Aptitude Test; DMN, Default Mode Network; MRI, magnetic resonance imaging; PMA, Primary Mental Abilities; SBM, surface-based morphometry; WMC, working memory capacity.

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modern human brain morphology may be associated with form changes in these medial parietal element (Bruner et al., 2014b).

In this study, we analyze the variation of the precuneal cortical thickness (CT) and cortical surface area (CSA) in a sample of modern adult humans by using surface-based morphometry (SBM), taking into account the overall brain measurements, sexual differences, and hemispheric asymmetries. CSA and CT are associated with cellular mechanisms which genetically and phenotypically show negligible correlations (Chen et al, 2013; Panizzon et al., 2009; Winkler et al., 2010). According to the radial-unit hypothesis, CSA is primarily determined by the number of radial columns perpendicular to the pial surface, and CT is determined by the horizontal layers in the cortical columns (Rakic, 2009). Individual differences in CSA depend upon the number of these columns, and individual differences in CT depend on the number of cells within a given column. Therefore, these two variables can give a reliable quantification of factors involved in cortical volume differences. We also evaluate, by using the shape groups evidenced in our previous study (Bruner et al., 2014a), whether precuneal thickness and surface area are involved in those main shape changes. Finally, we tested whether precuneal morphological variation is correlated with a set of psychometric scores tapping cognitive functions of increased complexity, namely processing speed, attention control, working memory, and intelligence. We have previously published analyses of correlation between brain geometry and standard cognitive variables (Bruner et al., 2011b; Martin-Loeches et al., 2013). Generally, most cognitive factors do not display patent associations with brain form, although some of them (attention control and processing speed, in particular) may show weak but consistent relationships with shape changes. Taking into consideration the neuroanatomical relevance of the precuneus in terms of both functional and spatial organization, the degree of correlation between its morphology and standard cognitive scores deserves close inspection.

EXPERIMENTAL PROCEDURES

Sample and magnetic resonance imaging (MRI) data collection

The sample includes MRI data from 104 adult individuals (45 males and 59 females; mean age and standard deviation 19.9 ± 1.7 years). Exclusion criteria included neurological or psychiatric illness, considering a history of serious head injury and substance abuse. Informed consent was obtained following the Helsinki guidelines, and the study was approved by the Ethics Committee of Universidad Autónoma de Madrid. MRIs were obtained with a 3T scanner (GEHC Waukesha, WI, USA, 3T Excite HDX) eight-channel coil. 3D: FSPGR with IR preparation pulse (repetition time (TR) 5.7 ms, echo time (TE) 2.4 ms, inversion time (TI) 750 ms, flip angle 12), with sagittal sections of 0.8-mm thickness, full brain coverage (220 slices), matrix 266 × 266, Field of View (FOV) 24 (isotropic voxels 0.7 cm^3).

SBM

MR images were submitted to the CIVET 1.1.9 pipeline developed at the Montreal Neurological Institute (Ad-Dab'bagh et al., 2006). SBM was applied for computing CSA and CT, according to the following steps: (1) registration of the MR images to standardized MNI-Talairach space based on the ICBM152 template (Collins et al., 1994; Mazziotta et al., 1995; Talairach and Tournoux, 1988); (2) correction for non-uniformity artifacts using the N3 approach; (3) classification of the images in gray matter, white matter and cerebrospinal fluid; (4) generation of high-resolution hemispheric surfaces with 40.962 vertices each; (5) registration of surfaces to a high resolution average surface template; (6) application of a reverse of step 'a' allowing surface or thickness estimations in native space for each subject; (7) smoothing data using 20-mm kernel for CT and 40-mm kernel for CSA; (8) computation of surface and thickness values at each vertex (see Karama et al. 2009, 2011 for further details). Finally, we delimited the region corresponding to the precuneus in the standard template using as approximate boundaries the subparietal sulcus, the marginal branch of the cingulate sulcus, and the parieto-occipital sulcus (Fig. 1), and applied a mask to compute the brain indices for the region of interest (ROI) only. This analysis was performed with the SurfStat toolbox designed for MATLAB (The MathWorks, Inc. - Natick, Massachusetts, USA)). Mean CT and total CSA were calculated for the left and right precuneus for each subject. These absolute non-normalized volumetric values were analyzed in the sample, and regressed onto the shape vector obtained in the previous study after geometric registration and size normalization.

Psychometric tests

We also evaluated the association of precuneal shape, CT, and CSA with a set of cognitive factors: (1) abstract-fluid intelligence (Gf) measures the complexity level that subjects can resolve in situations at which previous knowledge is irrelevant. Gf was measured with Raven Advanced Progressive Matrices Test (RAPM), the inductive reasoning subtest from the Primary Mental Abilities (PMA) battery (PMA-R), and the abstract reasoning subtest from the Differential Aptitude Test (DAT) battery (DAT-AR); (2) verbal-crystallized intelligence (Gc) is considered as the ability to face academic types of skills and knowledge, such reading or math. Gc was defined by the vocabulary subtests from the PMA (PMA-V), the verbal reasoning subtest from the DAT (DAT-VR), and the numerical reasoning subtest from the DAT (DAT-NR); (3) visuospatial intelligence (Gv) is involved in the construction, temporary retention, and manipulation of mental images. Gv was measured by the rotation of solid figures test, the mental rotation subtest from the PMA (PMA-S), and the spatial relations subtest from the DAT (DAT-SR); (4) working memory capacity (WMC) captures the ability for temporarily store-varied amounts of information while facing a concurrent processing requirement. WMC was defined by the reading span, computation span, and dot matrix tasks; (5) attention control was measured as the