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Midsagittal brain variation among non-human primates: insights into evolutionary expansion of the human precuneus

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Abstract

The precuneus is a major element of the superior parietal lobule, positioned on the medial side of the hemisphere and reaching the dorsal surface of the brain. It is a crucial functional region for visuospatial integration, visual imagery, and body coordination. Previously, we argued that the precuneus expanded in recent human evolution, based on a combination of paleontological, comparative, and intra-specific evidence from fossil and modern human endocasts as well as from human and chimpanzee brains. The longitudinal proportions of this region are a major source of anatomical variation among adult humans, and the main characteristic differentiating human midsagittal brain morphology from that of our closest living primate relative, the chimpanzee, being much larger in Homo sapiens. In the current shape analysis, we examine precuneus variation in non-human primates through landmark-based models, to evaluate the general pattern of variability in non-human primates, and to test whether precuneus proportions are influenced by allometric effects of brain size. Results show that precuneus proportions do not covary with brain size, and that the main difference between monkeys and apes involves a vertical expansion of the frontal and occipital regions in apes. Such differences might reflect differences in brain proportions or differences in cranial architecture. In this sample, precuneus variation is apparently not influenced by phylogenetic or allometric factors, but does vary consistently within species, at least in chimpanzees and macaques. This result further supports the hypothesis that precuneus expansion in modern humans is not merely a consequence of increasing brain size or of allometric scaling, but rather represents a species-specific morphological change in our lineage.
Keywords
precuneus; geometric morphometrics; brain morphology; macaques; apes

Introduction
Positioned at the medial cortical surface, the precuneus constitutes the medial portion of the parietal lobe, juxtaposed to the falx cerebri and extending onto the dorsal surface of the upper parietal lobule. In primates, it is delimited anteriorly by the marginal ramus of the cingulate sulcus, posteriorly by the parieto-occipital sulcus, and inferiorly by the subparietal sulcus [Cavanna and Trimble, 2006; Margulies et al., 2009]. Research on the precuneus has accelerated in the past decade due to development of non-invasive medical imaging techniques, namely MRI, fMRI, and PET. Functional studies have revealed that the precuneus is involved in a variety of functions associated with self-perception and visual imagery [Lou et al., 2004; Land, 2014], processing of spatial working memory [Wallentin et al., 2006, 2008], and memory retrieval (recognition of familiar faces [Gobbini and Haxby, 2007; Lee et al., 2013]; episodic memory [Vannini et al., 2011]; recognition memory [Hassabis and Maguire, 2009] autobiographical memory [Freton et al., 2014]). Moreover, the precuneus is a functional core of the Default Mode Network, a set of interconnected cortical areas that is active at rest [Raichle et al., 2001; Tomasi and Volkow, 2010; Utevsky et al., 2014], and it is a crucial hub of large-scale brain connectivity [Hagmann et al., 2008; Li et al., 2013; Reus et al., 2014]. Therefore, the precuneus is a region that is both structurally and functionally central for integrating multiple neural systems, and is comprised of different sub-regions involved in distinct cognitive functions [Margulies et al., 2009; Zang and Li 2012].

Adult humans display marked intraspecific variability in precuneus anatomy and morphology. When dealing with midsagittal brain geometry, the longitudinal proportions of the precuneus represent the main factor of variation among adult humans [Bruner et al., 2014a], by virtue of differences in cortical surface area [Bruner et al., 2015]. In adult humans, having a larger precuneus is partially associated with additional sulci, and with an expansion of its anterior-dorsal region [Bruner et al., 2017], corresponding in location to parietal area 7a [Scheperjans et al., 2008].

The histological and functional bases of this variation are not known, and changes in precuneus proportions are apparently not correlated with broad standard psychometric scores [Bruner et al., 2015]. Recent comparisons of humans and nonhuman primates using task-based and resting-state functional neuroimaging, as well as functional-connectivity MRI, indicate that these species share many features of precuneus organization [Rilling et al., 2007; Vincent et al., 2007; Kojima et al., 2009; Margulies et al., 2009; Barks et al., 2015; Caminiti et al., 2015]. Nevertheless, in addition to the marked intra-specific variation in humans, two observations suggest possibly significant evolutionary changes in humans. First, when comparing midsagittal brain morphology in humans and chimpanzees, the main difference is that Homo sapiens has a much larger precuneus in terms of absolute and relative size [Bruner et al., 2016]. Second, when comparing brain morphology in modern
and extinct human species, such as Neandertals, the main difference is a patent enlargement in *Homo sapiens* of the dorsal parietal surface, in a position that matches the precuneus longitudinal expansion [Bruner et al., 2003, 2014b; Bruner, 2004].

The precuneus morphology of non-human primates has not yet been analyzed quantitatively, and taking into account the large size of the human brain, it remains to be determined whether human precuneus enlargement is due to allometric patterns and scaling rules associated with the encephalization process. In this study, we analyze the shape variation of the precuneus in monkeys and apes, with the dual goals of investigating this cortical element in non-human primates, and of testing possible allometric patterns driving its morphological variability.

**Material and Methods**

The sample was composed of 42 non-human primate MRI scans from four species of monkeys and five species of apes (table 1). Specimens are all adults, and sex is not considered in the current survey. For this study, we used existing MRI databases described previously [Rilling and Insel, 1998, 1999; Rilling and Seligman, 2002; Chen et al., 2013; available at http://www.chimpanzeebrain.org], scanned at 1.5T, except for 10 chimpanzees which were scanned at 3T. MRI images were first reoriented using Nudge in FSL (https://fsl.fmrib.ox.ac.uk) so that the most anterior and the most posterior points were oriented in the horizontal plane, and the sagittal plane was parallel to the interhemispheric fissure of the brain. For 10 chimpanzees scanned separately at 3T, brain images were aligned to a chimpanzee brain template [Bruner et al., 2016] using rigid body linear registration with 6 degrees of freedom, so that the sagittal plane was parallel to the interhemispheric fissure of the brain. The reoriented images were then resampled to a consistent spatial resolution of 0.8 mm isotropic (for all apes except gibbons) or 0.5 mm isotropic (for all monkeys and gibbons). Each individual brain was then visualized in FSLVIEW and snapshots were taken for the first three sagittal slices in both hemispheres. These three slices were then joined in a single scout view by averaging the grayscale values into a single two-dimensional image, to effectively display the midsagittal brain gross morphology while limiting local noise [Pereira-Pedro and Bruner, 2016]. Shape variation of the midsagittal morphology was analyzed following the principles of geometric morphometrics [Zelditch et al., 2004]. We chose a set of 14 landmarks and semi-landmarks (Fig. 1a) in accordance with previous studies [Bruner et al., 2014a, 2016]: optic chiasm (Op), thalamus center (Th), center of the genu (Ge) and splenium (Sp) of the corpus callosum, frontal pole (FP; anterior-most point), marginal ramus of the cingulate sulcus (RCl), central point of the subparietal sulcus (Ss), external (PO) and internal (POi) extremes of the parieto-occipital sulcus, and occipito-cerebellar boundary (Oc). According to the current knowledge on these anatomical areas, all these points are considered to be homologous in monkeys and apes. The frontal curvature was sampled by three equally-distant semi-landmarks from the frontal pole to the precuneus. A semi-landmark was also sampled at 50% of the occipital curvature. Both hemispheres were digitized and then averaged. Landmark sets were scaled to the unitary size, translated to the same centroid, and rotated through Procrustes registration, minimizing the distance between corresponding landmarks [Bookstein, 1991]. The resulting shape coordinates were used for multivariate analyses. A first analysis considered species-average shapes, to provide
a general perspective on the morphological variation in primates. Shape patterns of variation were analyzed through Principal Component Analysis (PCA). Allometry was tested by multivariate regression of shape variables versus brain volume, so as to identify possible correlations between midsagittal morphology and whole brain size. For this survey we used species average values of brain volume published in Rilling and Seligman [2002]. A second analysis considered only chimpanzees and macaques, which are the only two groups in our sample with a number of specimens that allows intra-specific considerations. This second analysis is useful to compare two species with marked brain size differences. Geometric morphometrics were computed with PAST [Hammer et al., 2001] and MorphoJ [Klingenberg, 2011].

Results

Following PCA of the species average shapes, there was only one component above a threshold of random variation (Fig. 1b,c). This principal component explained 60% of the total variance, distributing species along a vector from capuchins to orangutans, associated with a generalized vertical stretching of the whole brain, which becomes rounder (Fig. 1d). This vector separates monkeys and apes, with gibbons and gorillas in an intermediate position. PC2 was roughly at the border with the threshold of normal random variation, explaining 19% of the variance (Fig. 1b,c), and may be worth mentioning. It mainly separated orangutans and capuchins from baboons: the former displayed relatively shorter length of the dorsal precuneus, and relatively larger length at the retrosplenial cortex (Fig. 1e), while the latter showed the opposite situation. When all specimens were analyzed together (data not shown), PC1 remained the same as in the previous analysis computed on mean species, but PC2 was strictly associated with precuneus dorsal length. However, most of the species analyzed in this survey include too few specimens, and hence the information on intra-specific variation was not sufficiently stable or reliable to merit robust conclusions.

Brain volume explained 45.5% of the whole shape variation (P = 0.008). The shape pattern associated with increasing brain size was the same as PC1 (Fig. 2a), and brain size was highly correlated with this vector (Fig.2b; R=0.87; R²=0.75; P-value for permutation test = 0.007). According to this allometric pattern, there was a tendency for smaller-brained monkeys to have flatter brains, and for the larger-brained great apes to have rounder brains. Gibbons and gorillas departed from this general trend falling outside the 95% confidence interval, the former showing a rounder brain relative to the small-brained monkeys, and the latter showing a more elongated brain compared with other apes.

When analyzing only chimpanzee and macaque specimens, PC1 explained 54% of the shape variation, and it separated the two species by a discrete morphological gap (Fig. 3a,b). This component was similar to the previous one, being associated with increasing rounder shape (from macaques to chimpanzees) because of bulging of the frontal curve and vertical stretching of the occipital morphology (Fig. 3c). PC2 (13%) was borderline relative to the threshold of random variation, and hence it was less consistent in terms of stability. Nonetheless, it is worth noting that PC2 was related to intra-specific (individual) variation associated with precuneus dorsal expansion/reduction (Fig. 3d). That is, this second component suggested that precuneus variation is a relevant factor within both species, and to
a similar extent. A discriminant function between the two groups (Fig. 3e,f) showed that chimpanzees displayed a more curved frontal profile and relatively larger occipital lobes (p < 0.0001; Fig. 3g).

Discussion

In humans, the longitudinal extent of the precuneus represents a major source of individual variation in brain anatomy [Bruner et al., 2014a, 2015]. The precuneus is also proportionally much larger in humans than in chimpanzees, not only in terms of absolute size but also in its proportions relative to other cortical regions [Bruner et al., 2016], and the corresponding dorsal parietal areas are expanded in modern human endocasts when compared with those of extinct human species [Bruner et al., 2014b]. Precuneus proportions among adult humans are unrelated to brain size, excluding allometric factors as an explanation for intra-specific variation. Fossil evidence similarly suggests that allometry cannot explain differential parietal enlargement in Homo sapiens since Neandertals had similar brain volumes but flatter and shorter parietal surfaces compared with modern humans [Bruner et al., 2003]. However, it is not known if allometric factors can explain differences in precuneus relative size between humans and chimpanzees. To evaluate this possibility, in this survey we tested whether brain size increase in non-human primates is associated with increase of precuneus proportions. We analyzed midsagittal brain shape in a sample of apes and monkeys that includes diverse genera with distinct adaptations and a wide range of brain sizes, to investigate precuneus morphological variation in living non-human anthropoid primates, and to test whether interspecific variability can be explained by allometric effects.

Our shape analysis showed that the main pattern of midsagittal brain variation among primates involves the general shape of the braincase, distinguishing rounded versus elongated brains, with no apparent change of local brain proportions. This morphological factor separated monkeys from apes, ranging from cebids (the flattest) to orangutans (the roundest). This pattern was associated with brain size, except in gibbons, which have a small brain size (83 cc) but a rounder brain shape, and in gorillas, who have large brain size (397 cc) but a more elongated brain shape. Bienvenu and colleagues [2011] obtained similar results in great apes based on the 3D morphology of endocasts: gorillas displayed long and narrow endocrania, and orangutans exhibited short and wide brains, while chimpanzees and bonobos (and humans) were intermediate. In our study, gorillas and gibbons, despite their brain size differences, displayed a similar brain shape, at least according to this main pattern of variation. Similarity between these two species has also been observed by McNulty [2004] in a craniofacial analysis of extant apes. He found that, when adjusting for size, gorillas and gibbons were closest among extant apes, and equally distant from chimpanzees, and suggested this similarity in shape might be due retention of ancestral hominoid cranial morphology. Gibbons also display a subcortical brain shape which is similar to apes and departs from a possible allometric trend, suggesting that beyond size-related effects there are some probable phylogenetic effects [Bruner and Jeffery, 2007].

The fact that the main pattern of variation, which is partially size related, involves the general form of the braincase and without localized changes of brain proportions, suggests that this component is probably due to cranial constraints rather than changes in the relative
size of different brain regions. Cranial form in monkey and apes is influenced by posture and muscle attachments, cranial base constraints, and facial integration, influencing the general proportions of the braincase [Moss and Young, 1960; Shea, 1985; Lieberman et al., 2000; Bastir et al., 2010]. In this sense, the main neurocranial difference between and within species is represented by the ratio between length and width, ranging from long, narrow and more elongated ones (dolichocephalic), to short, wide and more rounded braincases (brachycephalic) a variation which is due to distinct morphogenetic and phenotypic factors [Zollikofer and Ponce de León, 2002]. Therefore, at least for the features analyzed through this shape model, allometric variation in brain shape is apparently attributable to changes in cranial form rather than local expansion or contraction of brain regions. A recent analysis has demonstrated an important association between cranial and endocranial variation in hominoids, further stressing the role of skull constraints on brain shape evolution [Zollikofer et al., 2017], as already suggested according to the principles of functional craniology [Enlow, 1990; Bastir et al., 2006; Bruner and Ripani, 2008]. Nonetheless, most constraints have been identified in the cranial base and face, not in the dorsal cranium, and most shape analyses of the ape brain have been put forward only in terms of overall geometry, without taking into consideration the contribution of different brain districts. Therefore, we cannot exclude that part of our shape variation can be also due to real changes of brain proportions, although this is difficult to assess when dealing with the midsagittal morphology alone. For example, there is evidence suggesting that apes evolved relatively and absolutely larger frontal lobes when compared with other primates [Semendeferi et al., 1997, 2002; Semendeferi and Damasio, 2002; Smaers and Soligo, 2013], and we therefore cannot exclude that the pattern of frontal bulging described in this study could also be associated, at least in part, with an actual enlargement of the frontal cortex. Our results also suggest that, at least when compared with macaques, chimpanzees display a relatively larger occipital region.

The situation of gorillas merits further discussion. Gorillas and chimpanzees share a large allometric component although gorillas display a marked projection of the facial block which longitudinally stretches the braincase [Shea, 1983; Bruner and Manzi, 2001; Mitteroecker et al., 2004]. In contrast, orangutans have a specialized cranial architecture, with a pronounced aiorhynchy (dorsal flexion on the facial block) leading to a globular braincase [Shea, 1985, Bruner et al., 2004]. In this study, however, gorilla, and not orangutan, departs from the allometric trend. It is therefore probable that this general trend can hide multiple independent trajectories. A finer regression analysis distinguishing sub-groups was, however, not feasible in this study because of the small number of species included and consequent lack of statistical power.

Beyond any species-specific assessment, it is important to emphasize that the precuneus does not display any apparent variation in its proportions across this sample of non-human primate genera, which varies greatly in brain size. Apart from a change in its orientation due to the brachycephalic versus dolichocephalic condition, there is no evidence of relative enlargement or reduction. The comparison between chimpanzee and macaques further highlights this result: chimpanzees have a brain size about four times that of macaques, but there is no evidence of changes in the precuneus general proportions.
Therefore, all the current evidence suggests that parietal expansion in modern humans is a specific feature of our evolutionary lineage, and not the secondary allometric consequence of large brain size. In adult modern humans, precuneus variation is not correlated with brain size [Bruner et al., 2014a, 2017]. Within the genus Homo, Neandertals had a similar brain size as modern humans, but they did not display any parietal longitudinal enlargement [Bruner et al., 2003]. Finally, taking into account variation across primate species, the larger precuneus in modern humans, when compared with chimpanzees [Bruner et al., 2016], cannot be explained by allometric variation associated with brain size (this study).

It is interesting to note that, as in humans, we found marked within-species (individual) variation in relative precuneus size in our small macaque and chimpanzee samples, a result that deserves additional investigation with larger samples. Thus, precuneus plasticity may be a major feature shared among primates. The further increase in modern humans could be interpreted as the expression of an intrinsic potential of the primate brain. Evolutionary changes often occur in the same direction of the greatest genotypic/phenotypic variance, because the latter constrains the former, or because both patterns undergo the same selective pressure, generating evolutionary “lines of least resistance” [Schluter, 1996]. Therefore, we must evaluate whether the precuneus has some intrinsic property, because of genetic or environmental factors, that make it particularly sensitive to individual variation. Surely, the fact that it is positioned between the frontal and occipital blocks makes it susceptible to spatial limitations and morphogenetic constraints. Nonetheless, it is worth noting that our study, like previous studies on the same topic, relies on anatomical landmarks associated with specific boundaries of brain regions. Therefore, the relative expansion or reduction of a specific brain region cannot be explained simply as a passive consequence of spatial adjustments, but must be associated with the proportional increase or decrease of some histological component (number or size of neurons, connections, glia, etc.).

As a cautionary note, we must stress that this general survey is based on a limited number of primate species, each represented by only a few specimens. Taxon-specific analyses on larger collections would provide additional evidence on other species or genera. In particular, grade shifts between genera are expected and must be investigated with robust statistical samples, properly representing intra-specific variability and correlations. Also, we recognize that the precuneus is formed by distinct areas or subareas [Schepersjans et al., 2008], and variations within and between taxa have yet to be investigated at this level of organization. It will be therefore essential to investigate the different contribution of these areas to the overall morphological variability. Unfortunately, most parcellation schemes are based on parameters (cells, connections, functions, or physiological properties) that are not identifiable through macroscopic analyses.

The precuneus is crucial for the integration of the body and environment, in terms of spatial coordination but also in terms of simulation and visual imagery [Cavanna and Trimble, 2006; Margulies et al., 2009; Land, 2014]. It is also crucial for the perception and interpretation of social structure [Peer et al., 2015]. It has a notable metabolic load and thermal load, and is associated with metabolic impairments and vulnerability to neurodegenerative processes like Alzheimer’s Disease [Zhang and Li, 2012; Bruner and Jacobs, 2013; Bruner et al., 2014b]. The evidence presented in this study further suggests
that its enlargement in modern humans is not likely to be a consequence of brain size increase, and may represent a localized and specific character of *Homo sapiens*. We should now evaluate the precise histological components involved, and the possible functional significance, of this distinctive human brain morphology.

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**References**


Fig. 1.
Landmark set used in the analysis (a). Only the first principal component is above the threshold of random variation, although the second component can be also considered, mostly taking into account that multiple-species samples are not expected to be normally distributed (b,c). PC1 separates monkey and apes and it is associated, in the latter group, with a pronounced vertical stretching of the frontal profile and with longitudinal stretching of the occipital lobe (d). The second principal component separates baboons from capuchins and orangutans, because of shortening of the precuneus dorsal length and stretching of the retrosplenial cortex (e). Labels: capuchins (cap); mangabeys (mag); rhesus monkeys (rhe); orangutans (org); baboons (bab); chimpanzees (chm); gibbons (gib); gorillas (gor); bonobos (bon)
baboons (bab); gibbons (gib); gorillas (gor); bonobos (bon); chimpanzees (chm); orangutans (org).
Fig. 2.
Shape variation associated with brain size increase (a) is similar to the pattern observed in PC1. Actually, there is a consistent correlation between brain volume and PC1 scores (b). Species as in Figure 1.
Fig. 3.
Comparison between chimpanzees and macaques: variation explained by each principal component (a); plot of the first two principal components (b); deformation grids displaying shape variation along PC1 (c) and PC2 (d); average shape of chimpanzees (e) and of rhesus monkeys (f) and difference between the two species, according to a discriminant function (g). In (b) and (g) rhesus monkeys are light blue and chimpanzees are dark blue. On the transformation grids red is expansion and blue is constriction.
Table 1

Sample included in the analysis.

<table>
<thead>
<tr>
<th>Species</th>
<th>N</th>
<th>Brain volume (cc)</th>
<th>Average resolution</th>
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</thead>
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<tr>
<td>Capuchin (Cebus apella)</td>
<td>3</td>
<td>66.5</td>
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<tr>
<td>Rhesus monkey (Macaca mulatta)</td>
<td>7</td>
<td>79.1</td>
<td>0.56</td>
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<tr>
<td>Mangabeys (Cercopithecus atys)</td>
<td>3</td>
<td>98.8</td>
<td>0.50</td>
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<tr>
<td>Baboons (Papio cynocephalus)</td>
<td>2</td>
<td>143.3</td>
<td>0.50</td>
</tr>
<tr>
<td>Gorillas (Gorilla gorilla)</td>
<td>2</td>
<td>397.3</td>
<td>0.70</td>
</tr>
<tr>
<td>Gibbons (Hylobates lar)</td>
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<td>83</td>
<td>0.52</td>
</tr>
<tr>
<td>Orangutans (Pongo pygmaeus)</td>
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<td>0.73</td>
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<td>Bonobos (Pan paniscus)</td>
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<tr>
<td>Chimpanzees (Pan troglodytes)</td>
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<td>0.75</td>
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</table>