Neurosurgical anatomy of the insular cortex

Diogo Cunha-Cabral[a], Susana M. Silva[a,b], Hélio Alves[a], Ricardo P. Vaz[a,b,c], Pedro A. Pereira[a,b], José P. Andrade[a,b,*]

[a] Department of Biomedicine, Unit of Anatomy, Faculty of Medicine, University of Porto, Alameda Professor Hernâni Monteiro, 4200-319, Porto, Portugal
[b] Center for Health Technology and Services Research (CINTESIS), Rua Dr. Plácido da Costa, s/n, 4200-450, Porto, Portugal
[c] Otorhinolaryngology Department, Centro Hospitalar Universitário S. João, EPE, Alameda Professor Hernâni Monteiro, 4200-319, Porto, Portugal

ARTICLE INFO

ABSTRACT

Objective: The purpose of this study was to clarify the morphology of the insular cortex focusing not only on the shape of the insula, but also on sulcal and gyral organization.

Patients and methods: Sixty formalin-fixed adult brain hemispheres had their insula exposed and photographed. The dimensions of each gyrus and sulcus were measured using an image analysis software. The morphometric data obtained was statistically analysed.

Results: The insular cortex shape alternates between triangular and trapezoid, being the triangular shape the most common (75%). The angle between the posterior and inferior peri-insular sulcus in the trapezoid insulae had a mean range of 131.17° (SD = 12.277). A minimum of 3 and a maximum of 6 insular gyri were observed, being 5 the most common total number of gyri observed. The accessory gyrus was present in 66% of the insulae and well-developed in 38% of the cases. A statistical association between the number of gyri in the posterior lobe and the presence of a novel gyrus or a more developed accessory gyrus in the anterior lobe was found (P = 0.006). The posterior short gyrus was the longest of the short gyri (P < 0.001), followed by the anterior short gyrus (P < 0.001). The anterior long gyrus was the largest of the long gyri (P = 0.003). The contribution of each of the short gyri to the formation of the insular apex was inconstant. The most common observed apex arrangement was the combination of the anterior and of the middle short gyri.

Conclusions: This study makes a strong contribution to the understanding of the insular cortex anatomy, allowing neurosurgeons to be more capable to decide the best approach to this cortical area.

1. Introduction

The insula has been the focus of neuroanatomist´s attention for a long time. The first signs of the awareness of the presence of this structure dates from the 16th century as seen in Andreas Vesalius drawings [1]. However, it was only in 1809 that the name insula was attributed by Johann Christian Reil who first described its morphology (Reil, 1809; cited in Mavridis et al., 2011) [2]. Since then, a large amount of studies have been published regarding its embryology, morphology, connections and functions [3,4].

Due to the close association with the limbic system, the insula is classified as a paralimbic structure [5,6]. It is the first cortical area to develop and, during early fetal development it is localized in the superolateral region of the telencephalic vesicle [5,7–10]. In the next stage of development, the insular cortex is completely enclosed by surrounding cerebral gyri due to their rapid growth [2,5,11].

Afterwards, insular sulcal and gyral development begins at 17 gestational weeks and is completed at 28 gestational weeks [7].

Traditionally, the insular cortex has been described as a triangular structure defined by three peri-insular sulci and a central insular sulcus that divides the insula into an anterior lobe and a posterior lobe [11–15]. Recently, some authors suggested that the insula has a trapezoid shape that is delimited by four peri-insular sulci [16,17]. Despite the variation in the number of gyri in each lobe, the anterior lobe is usually composed by three gyri (anterior, middle and posterior short insular gyri) separated by the short insular sulcus and the pre-central insular sulcus, and a variable accessory gyrus. The posterior lobe normally only has two gyri (anterior and posterior long insular gyri) separated from each other by the post-central insular sulcus [14,15,18–20]. Functionally, the insular cortex plays an important role in cognitive processes [21] like pain processing [22–24], language and speech production [8,26,27], and processing of auditory stimuli [6]. It

is also involved in the regulation of autonomic responses like the cardiovascular function [25,26] and gustatory stimuli [27–29], and other visceromotor and viscerosensitive responses [5,28,30].

The descriptive anatomy of the insula is important in several medical fields, namely neurosurgery and neuroimaging. The use of correct and adequate terminology, a good understanding of the insular morphology and, more important, of the possible anatomical variations, is the base for accurate interpretation of images and for the precise development of surgical techniques [31]. In fact, not only the insula is the target of procedures addressing insular epilepsy or insular gliomas, but it is also seen as an important neurosurgical route to access certain brain areas, due to its strategic position in the deepness of the sylvian fissure [32–36]. Given the importance of this brain structure and the increasing need for minimally invasive neurosurgical approaches that spare important functional areas, we aimed to describe the morphology of the insular cortex using morphometric methodologies in 60 formalin-fixed human hemispheres.

2. Material and methods

2.1. Brain collection

The study was approved by the Ethical Committee of the Centro Hospitalar Universitário São João/Faculty of Medicine of the University of Porto (nº 111/19). The body donations to the Unit of Anatomy of the Biomedicine Department of the Faculty of Medicine of the University of Porto were in accordance to the Portuguese Act 274/99. A 10% formalin solution was injected into the bodies through the femoral artery and after the fixation, the brains were removed from each cadaver as previously described in detail [37,38].

2.2. Photographic records

The morphology of the insular cortex was evaluated in 60 adult brain hemispheres. Each of the available hemispheres had its insular cortex exposed either by retracting or completely removing the opercular portions of the frontal, parietal and temporal lobes (Fig. 1B and 3 B). After accessing the insulae, it was photographed together with a metric scale ruler. For every insulae the images were obtained in a perpendicular plane to the area of interest.

2.3. Gyri and sulci anatomical classification and measurements

Based on the nomenclature used by Türe et al. [14] and Naidich et al. [15] and according to Hans et al. [20] the characterization of the photographed insular cortex was made. The shape of the insular cortex was described. Some insulae presented a trapezoid shape instead of the traditionally described triangular one. In these trapezoid insulae, the angle formed by the inferior and posterior peri-insular sulci, named posterior-inferior angle by Afif & Mertens [39] was measured (Fig. 1C). The total number of gyri and the number of gyri in each insula were also registered.

The classification of the gyri upper extremity morphology was based on the criteria proposed by Wysiadecki et al. [19]. Therefore, each gyrus was classified as bifid, branched or novel when the sulcus that split its top extended up to 30%, between 30 and 50% or more than 50% down the gyrus length, respectively (Figs. 1 and 3). For descriptive purposes, we considered both the bifid and the branched gyrus together as split gyrus.

To evaluate the presence of the accessory gyrus a similar principle was applied. Any gyrus that originated from the anterior aspect of the anterior short gyrus lower than one-third of its length was considered to be the accessory gyrus (Fig. 1C). The development of the accessory gyrus was also assessed. However, given the fact that 10 of the insulae had their accessory gyrus damaged, we decided to exclude those from our statistical analysis as their development could not be properly evaluated.

All the gyri had their length and width measured from the obtained pictures using the *ImageJ* software (Fiji 1.46, National Institutes of Health, Bethesda, Maryland) [40]. The length of the gyri was measured from its upper limit to its base. To avoid falsely increased width measurements because of the gyri bifurcation, they were taken in the middle of each gyrus. The length of the sulci separating the adjacent gyrus was measured from the top of the main gyrus to the end-point of the sulcus (Figs. 1C and 3 C). All the present gyri had their degree of development visually evaluated as well-developed (reaching the convex surface of the insula), underdeveloped (not reaching the convex surface of the insula) or as hypoplastic (at the level of the adjacent gyrus bases) [19].

Besides the sulci length, we also determined their development based on their deepness and assessed whether they had their path interrupted by any stalk from the adjacent gyri or not. The contribution of the different gyri to the formation of the apex and the pole of the posterior lobule was also observed and registered.

2.4. Statistical analysis

For descriptive purposes we used counts and proportions for categorical variables and means and standard deviations for continuous variables. We compared the length and width of the several insular gyri and sulci; as these anatomical structures belonged to the same cerebral hemisphere, they could not be considered as independent samples, and so paired samples t tests were used to assess those measurements. A one-sample t test was performed to compare the mean range of the posterior-inferior angle in our study with the value previously reported by Afif & Mertens. Finally, chi-square tests were used to compare the degree of development of the insular gyri and sulci, and to assess the association between the number of posterior lobe gyri and the presence of a novel gyrus or a more developed accessory gyrus. The significance level was set at α = 0.05. Statistical analysis was conducted using SPSS statistical software package version 22 (SPSS inc., Chicago IL., USA).

3. Results

3.1. Insular cortex shape

Regarding the insular cortex shape, the insulae were classified as triangular in 75% (45/60) and trapezoid in 25% (25/60) of the cases (Figs. 1 and 2). In the latter cases, the mean range of the posterior-inferior angle was 131.17˚ (SD = 12.277). There was not a significant difference between our results (126˚, SD = 2) (*P* = 0.139) and the ones obtained by Afif & Mertens [39].

3.2. Insular sulci anatomy and measurements

In all the observed insulae (60/60) the anterior and posterior lobes were separated by the central sulcus which had its course interrupted in 18.3% of the cases (11/60). This important landmark was shown to be well-developed in 86.7% (52/60) of the analysed insulae, starting in the superior peri-insular sulcus in almost every hemisphere studied (98.3%; 59/60). In only one of the hemispheres analysed the central sulcus exhibited a different origin (1/60), starting from the posterior peri-insular sulcus. The mean length of the central sulcus was 2.81 cm (SD = 0.562). The remaining insular sulci showed a more variable presence. The short insular sulcus and the pre-central sulcus were present in almost every insula (96.7% and 98.3%, respectively) and the post-central sulcus was only observed in 76.7% of them. When compared, the post-central sulcus was significantly longer than the short insular sulcus and the pre-central sulcus (*P* < 0.001), whereas there were no differences between the mean length of the short insular sulcus and the pre-central sulcus (*P* = 0.056) (Table 1). There were no statistically significant differences in the degree of development of these
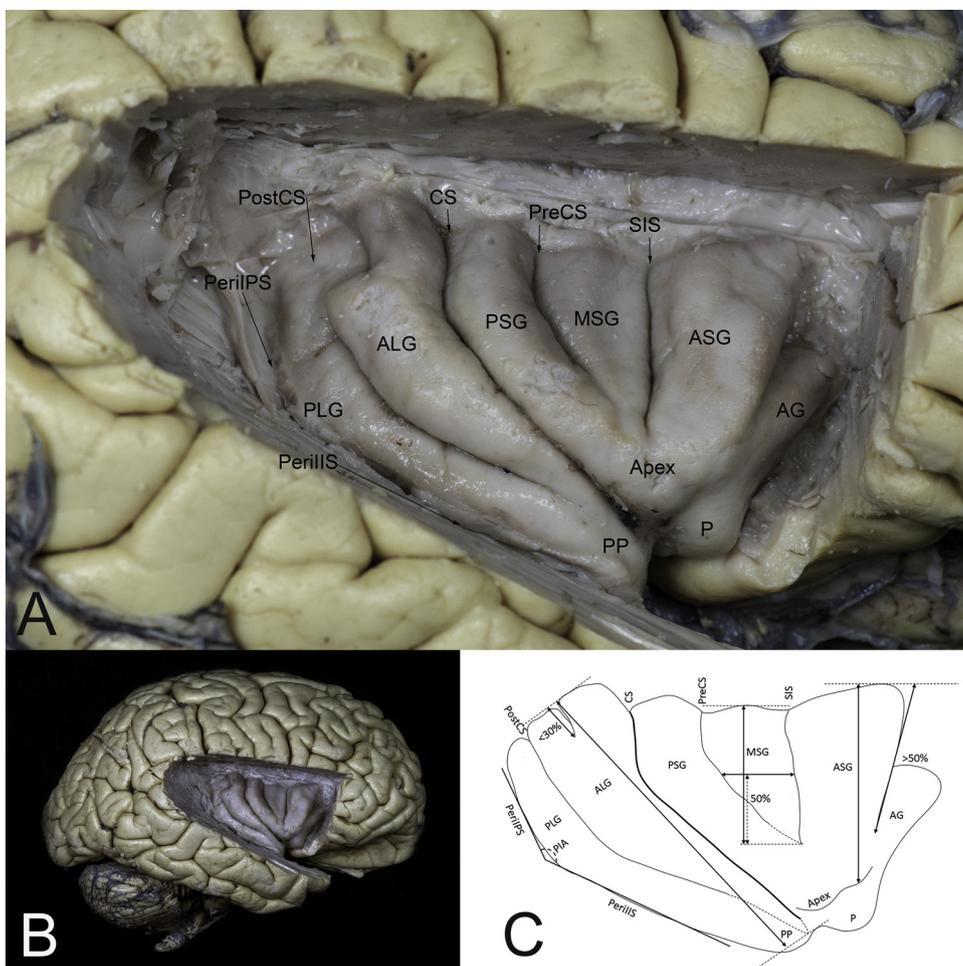
Fig. 1. Trapezoid insular cortex after the complete removal of the opercula. **A**: Example of a trapezoid insula delimited posteriorly by the posterior peri-insular sulcus (PeriIPS) and the inferior peri-insular sulcus (PeriIIS). The accessory gyrus (AG) is visualized on the anterior aspect of the anterior short gyrus (ASG). The anterior long gyrus (ALG) is bifid given its upper edge morphology. The apex of this specimen is formed by the ASG and the posterior short gyrus (PSG). The posterior lobe pole (PP) was formed by both the ALG and the posterior long gyrus (PLG). **B**: Lateral view of the right hemisphere with the opercula removed. **C**: Schematic representation of the insular cortex presented in A. The range of the posterior-inferior angle (PIA) between the PeriIPS and the PeriIIS was registered. The gyrus on the anterior aspect of the ASG was considered as the AG because it originated more than 30% down the ASG length. Every sulcus had its length measured from the top of the main gyrus to the end-point of the sulcus. The length of every gyri was measured from its upper limit to its base, whereas the width was measured at middle height of the gyrus.

The ALG is classified as bifid because its upper extremity is split by a sulcus that extends up to 30% down its length. CS – central sulcus; MSG – middle short gyrus; P – pole of the insula; PostCS – postcentral sulcus; PreCS – precentral sulcus; SIS – short insular sulcus.

sulcus ($P = 0.929$).

3.3. Insular gyri anatomy and measurements

The total number of the insular gyri varied between 3 and 6, with 5 gyri being the most common pattern (61.7%). In the anterior lobe the minimum and the maximum number of gyri observed were 2 and 5, respectively. However, the most prevalent number of short gyri were 3 (45%) and 4 (48.3%). The pattern that was more often verified in the posterior lobe was the presence of 2 long gyri (76.7%) (Table 2).

In the anterior lobe, the anterior short gyrus and the posterior short gyrus were always present (60/60). On the other hand, the middle short gyrus was observed in 93.3% of the cases (56/60). The anterior short gyrus and the posterior short gyrus appeared to be well-developed in almost all the observed insulae (93.3% and 98.3%, respectively), whereas the middle short gyrus was considered well-developed in only 41.7% (25/60) of the cases. In 18.3% (11/60) of the insulae this gyrus was hypoplastic. These differences in the degree of development of the anterior lobe gyri were statistically significant ($P < 0.001$). The middle short gyrus originated from the posterior short gyrus in 40% (24/60) of
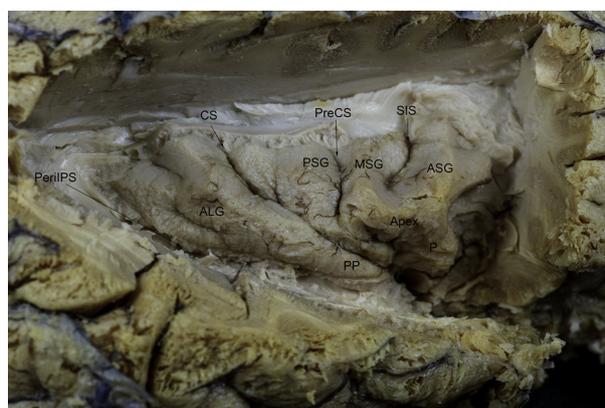
Fig. 2. Triangular insular cortex. Left: Triangular insular specimen delimited posteriorly by the posterior peri-insular sulcus (PeriIPS) alone. This insular cortex has a single posterior lobe gyrus which shows a bifid morphology. Right: Schematic representation of the example presented in the picture on the left. ALG – anterior long gyrus; ASG – anterior short gyrus; CS – central sulcus; MSG – middle short gyrus; PSG – posterior short gyrus; SIS – short insular sulcus; P – pole of the insula; PP – pole of the posterior lobe; PreCS – precentral sulcus.
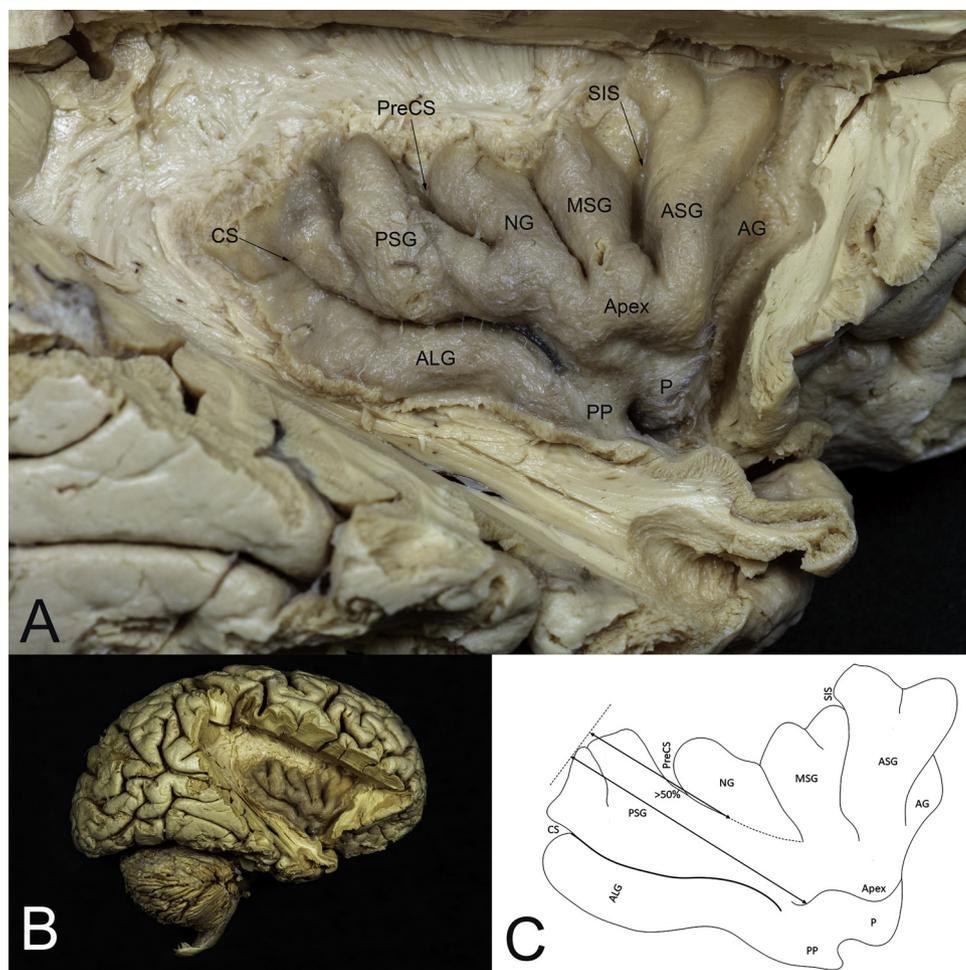
Fig. 3. Insular cortex displaying six gyri. **A:** Example of an insular cortex with only one long gyrus and five short gyri. The accessory gyrus (AG) is the first of the short gyri. A novel gyrus (NG) is also observed in the anterior lobe. **B:** Lateral view of the right hemisphere having the insula exposed. **C:** Schematic representation of the insular cortex showed in A. The gyrus adjacent to the posterior short gyrus (PSG) is classified as being a NG because it originates more than 50% down the length of the PSG. ALG – anterior long gyrus; ASG - anterior short gyrus; CS – central sulcus; MSG - middle short gyrus; P – pole of the insula; PP – pole of the posterior lobe; PreCS – precentral sulcus; SIS – short insular sulcus.

Table 1
Paired *t*-test results on the short gyri length and width comparison and length of sulci.

	Mean difference (95% CI)	p value
post-CS vs SIS	0.899 (0.634; 1.164)	< 0.001
post-CS vs pre-CS	0.817 (0.564; 1.071)	< 0.001
pre-Cs vs SIS	0.116 (0.564; 1.071)	0.056
ASG vs MSG		
Length	0.377 (0.237; 0.517)	< 0.001
Width	− 0.792 (-0.90; 0.167)	0.077
PSG vs MSG		
Length	0.684 (0.544; 0.824)	< 0.001
Width	− 0.059 (-0.127; 0.008)	0.084
PSG vs ASG		
Length	0.317 (0.180; 0.454)	< 0.001
Width	0.007 (-0.060; 0.073)	0.843

ASG – Anterior short gyrus; MSG – middle short gyrus; post-CS – post-central insular sulcus; pre-CS – pre-central insular sulcus; PSG – posterior short gyrus; SIS – short insular sulcus.

Table 2
Total number of gyri in the insulae and in each of its lobes.

	Insula total gyri	Anterior lobe gyri	Posterior lobe gyri
Mean (SD)	5.20 (0.632)	3.47 (0.623)	1.77 (0.427)
Minimum	3	2	1
Maximum	6	5	2
Frequencies	3 - 1.7% (1/60)	2 - 3.0% (3/60)	1 - 23.3% (14/60)
	4 - 6.7% (4/60)	3 - 45% (27/60)	2 - 76.7% (46/60)
	5 - 61.7% (37/60)	4 - 48.3% (29/60)	
	6 - 30% (18/60)	5 - 1.7% (1/60)	

Table 3
Gyri measurement results.

	Mean length (SD)	Mean width (SD)
ASG	1.99 (0.474)	0.76 (0.208)
MSG	1.61 (0.407)	0.83 (0.255)
PSG	2.31 (0.386)	0.77 (0.170)
ALG	3.04 (0.549)	0.66 (0.158)
PLG	3.11 (0.771)	0.57 (0.167)

ALG – anterior long gyrus; ASG – Anterior short gyrus; MSG – middle short gyrus; PLG – posterior long gyrus; PSG – posterior short gyrus.

the cases and from the anterior short gyrus in a smaller percentage of insulae (16.7%, 10/60). In the remaining cases, it was isolated (31.7%), or it was impossible to determine its origin (3.3%). The results of the short gyri measurements are presented in Table 3. Statistically, the posterior short gyrus was the longest gyrus (*P* < 0.001) and the anterior short gyrus was longer than the middle short gyrus (*P* < 0.001). In opposition, none of the gyrus demonstrated to be larger than the other (Table 1).

The accessory gyrus was present in 66% (33/50) of the cases (Figs. 1A and 3 C). When present, it appeared to be well-developed in

19 of the 50 (38%) insulae that were available for this analysis with a mean length and width of 1.15 cm (SD = 0.399) and 0.49 cm (SD = 0.197), respectively. In our sample, the transverse gyrus also demonstrated a variable presence being identifiable in 63.3% of the cases (38/60). In those cases where the anterior lobe had a novel gyrus (10%), it had a mean length of 1.29 cm (SD = 0.462) and a mean width

Table 4
Morphology of the upper extremity of the insular gyri.

	ASG	MSG	PSG	ALG	PLG
Isolated	76.7% (46/60)	90.7% (49/54)	70% (42/60)	65% (39/60)	90.7% (39/43)
Split gyrus (Bifid + Ramified)	23.3% (14/60)	9.3% (5/54)	30% (18/60)	35% (21/60)	9.3% (4/43)

ALG - anterior long gyrus; ASG - Anterior short gyrus; MSG - middle short gyrus; PLG - posterior long gyrus; PSG - posterior short gyrus.

of 0.58 cm (SD = 0.078), beginning mainly in the posterior short gyrus (6.7%). An association between the number of the posterior lobe gyri and the presence of a novel gyrus or a more developed accessory gyrus was described. In fact, in 78.6% of the cases that the posterior lobe presented only one long gyrus, there was a novel gyrus in the anterior lobe or the accessory gyrus was well-developed (Fig. 3A and C), compared to 35.1% where were identified two long gyri (P = 0.006).

The posterior lobe was always composed by the anterior long gyrus (60/60). However, the posterior long gyrus only contributed to the formation of the posterior lobe in 73.3% (44/60) of the cases and in 5% (3/60) it originated from the anterior long gyrus. The results related to the long gyri measurements are presented in Table 3. There were no significant differences between the length of both gyri (P = 0.239), though the width of the anterior long gyrus was significantly superior (P = 0.033). The posterior long gyrus had also a more inconsistent development, being well-developed in 86.4% of the cases compared to the 100% of the anterior long gyrus (P = 0.005).

In Table 4, the results from the observation of the insular gyri upper extremity morphology were presented. The splitting of the upper extremity of the gyrus was more often observed in the anterior short gyrus, posterior short gyrus and anterior long gyrus when compared to the anterior short gyrus and posterior long gyrus (P < 0.011).

The gyri that more often contributed to the insular apex formation were the anterior short gyrus and middle short gyrus together (28.3%) (Fig. 3A). While the combination of the anterior short gyrus followed by the posterior short gyrus (26.7%) (Fig. 1A) was also observed. There were likewise other patterns of combinations that equally contributed to the insular apex formation, namely the middle short gyrus + posterior short gyrus (20%), the anterior short gyrus alone (13.3%), the middle short gyrus alone (10%) and finally the posterior short gyrus alone (1.7%).

We identified that the posterior lobe pole was formed by both anterior long gyrus and posterior long gyrus (Fig. 1A) in 45% of the insulae (27/60) and by the anterior long gyrus or the posterior long gyrus alone in 36.7% (22/60) and 18.3% (11/60), respectively.

4. Discussion

The present work is based on the observation of a total of 60 insulae. To our knowledge, this study takes part in a group of morphometric studies with the largest number of insulae analysed. Although a limitation of the present study is the absence of data regarding age, sex and detailed medical history of the body donors, the precise morphometric quantification and statistical analysis of the insular anatomy and the characterization of its shape were greatly achieved by studying this large sample.

The traditional concept of a triangular insular shape was contradicted for the first time by Afif & Mertens [39]. Unlike many authors that had previously described the insula as triangular and delineated by three peri-insular sulci [2,11–14,41], Afif & Mertens [39] described the shape as being trapezoid in 100% of the insulae studied, naming the angle formed by the inferior and posterior peri-insular sulci as the posterior-inferior angle [16,39]. Nevertheless, our results demonstrate that the insula can either be triangular or trapezoid, being the triangular shape the most prevalent pattern (75% vs 25%). In those hemispheres in which the insula was trapezoid, the mean range of the posterior-inferior angle was 131.17° which was not significantly different from the value obtained by Afif & Mertens [39].

Taking into consideration the number of gyri, our results are somewhat consistent with the previous studies on this issue. The minimum total number of gyri that we observed was of 3 in one isolated case (1.7%). Preceding reports [2,11,12,15,19] described a minimum of 4 insular gyri while others [16,39] reported a minimum of 5 insular gyri. The maximum total number of gyri we described were 6, which was in accordance with most of the studies [15,16,19,39]. The utmost common total number of gyri identified was 5, a finding that is unanimously supported by the literature [2,12,14–16,19,39]. The minimum number of short gyri (2) is similar to those found by other researchers [2,11,12,15,19]. On the other hand, the maximum number of short gyri present in our sample was 5 (1/60), a result only obtained by Varnavas & Grand [12]. Our findings concerning the number of long gyri are also consistent with previous reports [2,11–13,15,19]. The discrete discrepancies on the number of gyri may be related to the criteria used for the classification of the accessory gyrus. In our study, we adopted the criteria proposed by Wysiadecki et al. [19] according to which a gyrus is defined as accessory gyrus if it originates from the anterior surface of the anterior short gyrus more than 30% down its length. If this condition was present, then the accessory gyrus was the first short gyrus of the anterior lobe. Our results corroborate those obtained by Wysiadecki et al. [19] (Table 5) demonstrating that the suggested classification criteria are simultaneously simple to applicate and adequate for descriptive purposes.

Amongst the short gyri, the middle short gyrus was the one that had a more variable degree of development as previously described [12,14,15,19]. Our results support this finding for the first time using a quantitative methodology. Similarly, in the posterior lobe, the posterior long gyrus showed a more inconsistent presence and development [11–13,19]. The present data shows a statistically significant lesser development of the posterior long gyrus when compared to the anterior long gyrus. The dimensions of each gyrus also deserved our attention. Our findings indicate that the posterior short gyrus is the longest of the short gyri, followed by the anterior short gyrus. Unlike Tanriover et al.

Table 5
Comparison of the results on the accessory gyrus (AG) presence and development with and without the criteria defined by Wysiadecki et al. [44].

		AG absent	AG underdeveloped	AG well developed
With Classification Criteria	Our Results 50 hemispheres	34% (17/50)	28% (14/50)	38% (19/50)
	Wysiadecki et al. [44] 50 hemispheres	30% (15/50)	36% (18/50)	34% (17/50)
Without Classification Criteria	Ribas et al. [33] 16 hemispheres	50% (8/16)	Present in 50% of the hemispheres (8/16)	
	Naidich et al. [25] 16 hemispheres	0% (0/16)	62.5% (10/16)	31.25% (5/16)
	Türe et al. [40] 50 hemispheres	18% (9/50)	34% (17/50)	48% (24/50)
	Tanriover et al. [38] 43 hemispheres	40% (17/43)	Present in 60% of the hemispheres (26/43)	

[13] that described the anterior short gyrus as being the largest of the anterior lobe gyri, we did not find any significant difference in the width of these gyri. A different result was obtained related to the width of the long gyri, as the anterior long gyrus demonstrated to be significantly larger than the posterior long gyrus, a feature previously described by Tanriover et al. [13].

The apex of the insula is defined as the most convex point of the insular cortex. This morphological feature is considered an important neurosurgical landmark. However, the high variability of gyri that contribute to its formation [11,15,19] makes it a poorly reliable landmark [11]. Our results strongly reinforce the idea that both, the anterior short gyrus and middle short gyrus, together often contribute to the insular apex formation in combination with other gyri.

Our study describes for the first time a significant association between the number of the posterior lobe gyri and the presence of a novel gyrus in the anterior lobe or a more developed accessory gyrus. In the insulae were a single long gyrus was described, a novel gyrus or a more developed accessory gyrus was more frequently identified. This information may point to an influence of the anterior lobe gyri in the development of the long gyri as a more developed anterior lobe could physically restrain the presence of a second gyrus in the posterior lobe. Data from embryological studies support this hypothesis by describing an earlier development of the short gyri when compared to the long gyri (22 gestational weeks vs 24 gestational weeks) [7]. Furthermore, we are in the opinion that the described pattern may strongly contribute in predicting the morphology of the posterior lobe of the insula.

The complex anatomy of insular cortex and its proximity to such important cortical areas like language, primary auditory and primary motor and sensory areas of the face, represent some of the determining reasons why the insula surgery is considered a major challenge for neurosurgeons [4,42]. The insular epilepsy surgery and the surgical resection of insular gliomas are good examples of how difficult procedures involving this cortical area, require careful preoperative planning and adequate intraoperative mapping and monitoring [43]. In fact, according to Mavridis et al. [2] when planning a surgery involving the insula, each patient anatomy should be determined in detail with a preoperative MRI. In their opinion, an increased gyri pattern (6 or 7) precludes a transylvian approach due to the greater volume and complex insular anatomy. In these cases, the transopercular approach was advisable [2]. On the other hand, if a decreased gyri pattern (3 and 4) was present which was related to a smaller insular volume and a simpler anatomy, a transylvian approach was preferable [2]. Indeed, the resection of insular gliomas represents a very demanding surgery, as these tumours often extend beyond the insula into nearby structures as white matter tracts. The insula is surrounded not only by association tracts such as the uncinate fascicle, the arcuate fascicle and the inferior fronto-occipital fascicle, but also by commissural and projection tracts like the anterior commissure and the internal capsule [43,44]. According to Duffau [44], the surgery of insular gliomas located in the posterior-superior quadrant of the insula (corresponding to Sanai Zone II) [45] should be considered troublesome due to its deeper placement in the Sylvian fissure and to its close relation with the posterior limb of the internal capsule, leading to lower resection rates [45]. Despite the major importance of functional imaging modalities and of intraoperative monitoring, particularly in Zone II gliomas surgeries, all neuroanatomical information achieved from basic studies should be considered imperative for neurosurgeons, as they would strongly benefit from information related to the anatomy of the region and its patterns of variability to foresee and overcome eventual obstacles.

5. Conclusion

It is extremely important for neurosurgeons to have a detailed information of the anatomy of the insula [2,4,36,42]. With this anatomical and quantitative study, we further contribute to this knowledge by providing important morphometric and accurate anatomic data from a large number of human insulae. This, in turn, can be useful for neurosurgeons to overcome the technical challenges associated with the insula surgical approach.

Declaration of Competing Interest

The authors wish to declare no conflicts of interests and no commercial or financial relationships.

Acknowledgements

References

[1] B.P. Shelley, M.R. Trimble, The insular lobe of Reil–its anatamico-functional, behavioural and neuropsychiatric attributes in humans–a review, World J. Biol. Psychiatry 5 (4) (2004) 176–200.

[2] I. Mavridis, E. Boviatsis, S. Anagnostopoulou, Exploring the neurosurgical anatomy of the human insula: a combined and comparative anatomic-radiologic study, Surg. Radiol. Anat. 33 (4) (2011) 319–328.

[3] A.W.K. Yeung, The 100 most cited papers concerning the insular cortex of the brain: a bibliometric analysis, Front. Hum. Neurosci. 12 (2018) 337.

[4] M. Turgut, C. Yurttaş, R.S. Tubbs, Island of Reil (Insula) in the Human Brain: Anatomical, Functional, Clinical and Surgical Aspects, Springer, 2018.

[5] F.G. Flynn, Anatomy of the insula functional and clinical correlates, Aphasiology 13 (1) (1999) 55–78.

[6] M.Y.S. Kalani, M.A. Kalani, R. Gwinn, B. Keogh, C. Victor, Embryological development of the human insula and its implications for the spread and resection of insular gliomas, Neurosurg. Focus 27 (2) (2009) E2.

[7] A. Afif, R. Bouvier, A. Buenerd, J. Trouillas, P. Mertens, Development of the human fetal insular cortex: study of the gyration from 13 to 28 gestational weeks, Brain Struct. Funct. 212 (3–4) (2007) 335–346.

[8] F. Keibel, F.P. Mall, Manual of Human Embryology, JB Lippincott Company, 1912.

[9] S. Kodam, Über die sogenannten Basalganglien, Morphogenetische und pathologisch-anatomische Untersuchunger, Schweiz Arch Neurol Psychiatr 18 (1926) 179–246.

[10] M.S. Wai, C. Shi, W. Kwong, L. Zhang, W.P. Lam, D.T. Yew, Development of the human insular cortex: differentiation, proliferation, cell death, and appearance of 5HT-2A receptors, Histochem. Cell Biol. 130 (6) (2008) 1199.

[11] E.C. Ribas, K. Yağmurlu, E. de Oliveira, G.C. Ribas, A. Rhoton Jr, Microsurgical anatomy of the central core of the brain, J. Neurosurg. (2017) 1–18.

[12] G.G. Varnavas, W. Grand, The insular cortex: morphological and vascular anatomic characteristics, Neurosurgery 44 (1) (1999) 127–136.

[13] N. Tanriover, A.L. Rhoton Jr, M. Kawashima, A.J. Ulm, A. Yasuda, Microsurgical anatomy of the insula and the sylvian fissure, J. Neurosurg. 100 (5) (2004) 891–922.

[14] U. Türe, D.C. Yasargil, O. Al-Mefty, M.G. Yasargil, Topographic anatomy of the insular region, J. Neurosurg. 90 (4) (1999) 720–733.

[15] T.P. Naidich, E. Kang, G.M. Fatterpekar, B.N. Delman, S.H. Gultekin, D. Wolfe, O. Ortiz, I. Yousry, M. Weismann, T.A. Yousry, The insula: anatomic study and MR imaging display at 1.5 T, AJNR Am. J. Neuroradiol. 25 (2) (2004) 222–232.

[16] A. Afif, D. Hoffmann, G. Becq, M. Guenot, M. Magnin, P. Mertens, MRI-based definition of a stereotactic two-dimensional template of the human insula, Stereotact. Funct. Neurosurg. 87 (6) (2009) 385–394.

[17] A. Afif, L. Minotti, P. Kahane, D. Hoffmann, Anatomofunctional organization of the insular cortex: a study using intracerebral electrical stimulation in epileptic patients, Epilepsia 51 (11) (2010) 2305–2315.

[18] A. Rosen, D.Q. Chen, D.J. Hayes, K.D. Davis, M. Hodaie, A neuroimaging strategy for the three-dimensional in vivo anatomical visualization and characterization of insular gyri, Stereotact. Funct. Neurosurg. 93 (4) (2015) 255–264.

[19] G. Wysiadecki, A. Malkiewicz, J. Rozniecki, M. Polguj, R. Haladaj, A. Zytkowski, M. Topol, Anatomical variations of the insular gyri: a morphological study and proposal of unified classification, Clin. Anat. 31 (3) (2018) 347–356.

[20] J. Hans, N. Tzourio-Mazoyer, J.K. Mai, Toward a common terminology for the gyri and sulci of the human cerebral cortex, Front. Neuroanat. 12 (2018).

[21] R.L. Perri, M. Berchicci, V. Bianco, D. Spinelli, F. Di Russo, Brain waves from an "isolated" cortex: contribution of the anterior insula to cognitive functions, Brain

Struct. Funct. 223 (3) (2018) 1343–1355.

[22] K. Ostrowsky, M. Magnin, P. Ryvlin, J. Isnard, M. Guenot, F. Mauguière, Representation of pain and somatic sensation in the human insula: a study of responses to direct electrical cortical stimulation, Cereb. Cortex 12 (4) (2002) 376–385.

[23] A. Afif, D. Hoffmann, L. Minotti, A.L. Benabid, P. Kahane, Middle short gyrus of the insula implicated in pain processing, Pain 138 (3) (2008) 546–555.

[24] C. Lu, T. Yang, H. Zhao, M. Zhang, F. Meng, H. Fu, Y. Xie, H. Xu, Insular cortex is critical for the perception, modulation, and chronification of pain, Neurosci. Bull. 32 (2) (2016) 191–201.

[25] M. Seeck, S. Zaim, V. Chaves-Vischer, O. Blanke, M. Maeder-Ingvar, M. Weissert, E. Roulet, Ictal bradycardia in a young child with focal cortical dysplasia in the right insular cortex, Eur. J. Paediatr. Neurol. 7 (4) (2003) 177–181.

[26] M.S. Hassanpour, W.K. Simmons, J.S. Feinstein, Q. Luo, R.C. Lapidus, J. Bodurka, M.P. Paulus, S.S. Khalsa, The insular cortex dynamically maps changes in cardiorespiratory interoception, Neuropsychopharmacology 43 (2) (2018) 426.

[27] D.-E. Bamiou, F.E. Musiek, L.M. Luxon, The insula (Island of Reil) and its role in auditory processing: literature review, Brain Res. Rev. 42 (2) (2003) 143–154.

[28] E.T. Rolls, Functions of the anterior insula in taste, autonomic, and related functions, Brain Cogn. 110 (2016) 4–19.

[29] S. Linsambarth, J. Stehberg, The Insular Cortex and Taste Novelty, Food Neophobia, Elsevier, 2018, pp. 129–145.

[30] J. Isnard, M. Guénot, M. Sindou, F. Mauguière, Clinical manifestations of insular lobe seizures: a stereo-electroencephalographic study, Epilepsia 45 (9) (2004) 1079–1090.

[31] H.J. Ten Donkelaar, J. Broman, P.E. Neumann, L. Puelles, A. Riva, R.S. Tubbs, D. Kachlik, Towards a terminologia neuroanatomica, Clin. Anat. 30 (2) (2017) 145–155.

[32] S. Mishra, R.C. Mishra, The transvlian trans-insular approach to lateral thalamic lesions, Neurol. India 60 (4) (2012) 385.

[33] M.B. Potts, E.F. Chang, W.L. Young, M.T. Lawton, U.B.A.S. Project, Transsylvian-transinsular approaches to the insula and basal ganglia: operative techniques and results with vascular lesions, Neurosurgery 70 (4) (2012) 824–834.

[34] S. Nagata, T. Sasaki, The transsylvian trans-limen insular approach to the crural, ambient and interpeduncular cisterns, Acta Neurochir. 147 (8) (2005) 863–869.

[35] H. Rafael, Transsylvian and transinsular approach, Turk. Neurosurg. 5 (3) (1995) 53–56.

[36] S.L. Hervey-Jumper, M.S. Berger, Insular glioma surgery: an evolution of thought and practice, J. Neurosurg. 130 (1) (2019) 9–16.

[37] S.M. Silva, J.P. Andrade, Neuroanatomy: the added value of the Klingler method, Ann. Anat.-Anatomischer Anzeiger 208 (2016) 187–193.

[38] P. Felle, A.K. Lockman, P. Kellaghan, Removal of the brain for teaching and examination, Clin. Anat. 8 (5) (1995) 363–365.

[39] A. Afif, P. Mertens, Description of sulcal organization of the insular cortex, Surg. Radiol. Anat. 32 (5) (2010) 491–498.

[40] C.A. Schneider, W.S. Rasband, K.W. Eliceiri, NIH Image to ImageJ: 25 years of image analysis, Nat. Methods 9 (7) (2012) 671–675.

[41] M. Guenot, J. Isnard, M. Sindou, Surgical Anatomy of the Insula, Advances and Technical Standards in Neurosurgery, Springer, 2004, pp. 265–288.

[42] F. Signorelli, J. Guyotat, K. Elisevich, G.M. Barbagallo, Review of current microsurgical management of insular gliomas, Acta Neurochir. 152 (1) (2010) 19–26.

[43] A. Tsitlakidis, N. Foroglou, Surgical Resection Techniques of Insular Gliomas, Epilepsy Surgery and Intrinsic Brain Tumor Surgery, Springer, 2019, pp. 245–259.

[44] H. Duffau, Surgery of Insular Gliomas, Intracranial Gliomas Part I-Surgery, Karger Publishers, 2018, pp. 173–185.

[45] N. Sanai, M.-Y. Polley, M.S. Berger, Insular glioma resection: assessment of patient morbidity, survival, and tumor progression, J. Neurosurg. 112 (1) (2010) 1–9.