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Diogo da Cunha Cabral

Neurosurgical anatomy of the insular cortex

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Neurosurgical anatomy of the insular cortex

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“As cousas árduas e lustrosas

Se alcançam com trabalho e com fadiga”

Luís Vaz de Camões, in Os Lusíadas, Canto IV

Este pequeno espaço reservado aos agradecimentos nunca será o suficiente para enaltecer o contributo dado por todos aqueles que me acompanharam neste pedaço de vida e me ajudaram a ultrapassar as dificuldades que no seu decurso se me depararam.

A toda a minha família, particularmente aos meus pais e irmãos, à Diana, aos meus amigos e a toda a Unidade de Anatomia, o meu mais profundo e sentido obrigado.

Neurosurgical anatomy of the insular cortex

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Running title: Anatomy of the insula

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 (Figs. 1B and 3B). 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 (Fig 1C and 3C). 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 2.81cm (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 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 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 3C). 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 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 (Figs. 3A and 3C), 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 the 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. [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 pre-operative 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.

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DISCLOSURE

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

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FIGURE CAPTIONS

Figure 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.

Figure 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 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.

Figure 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.

Figure 1

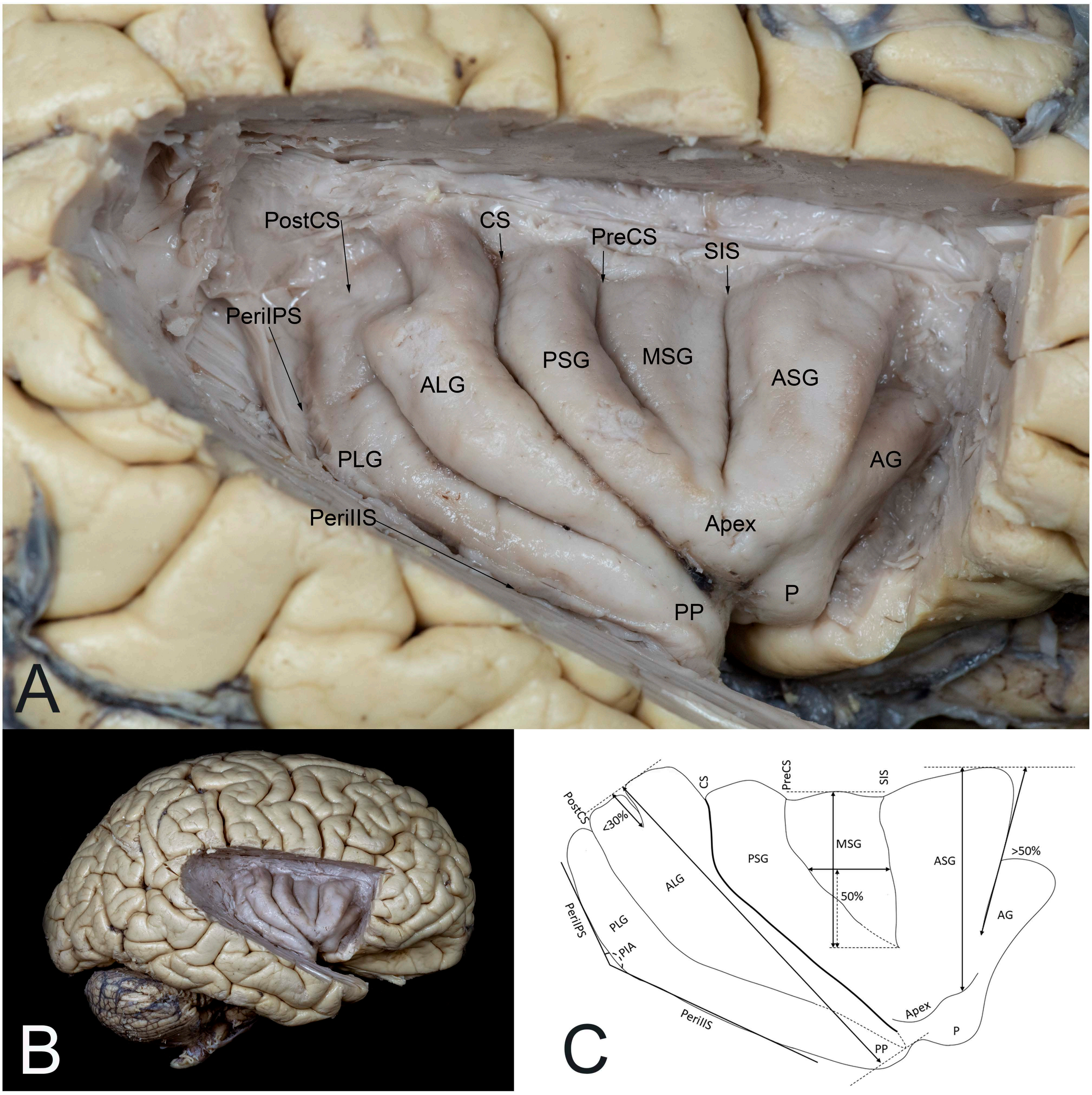
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Figure 2

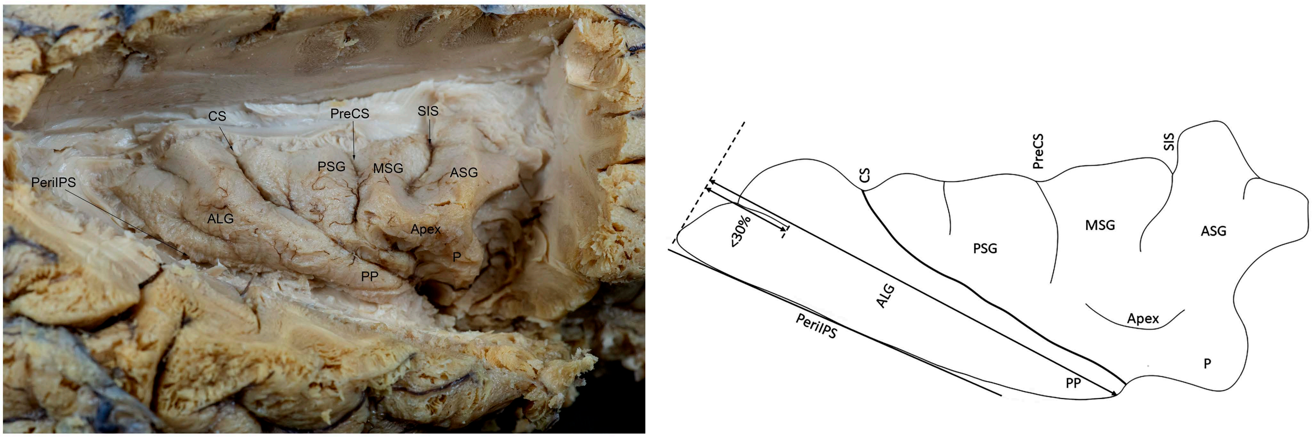
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Figure 3

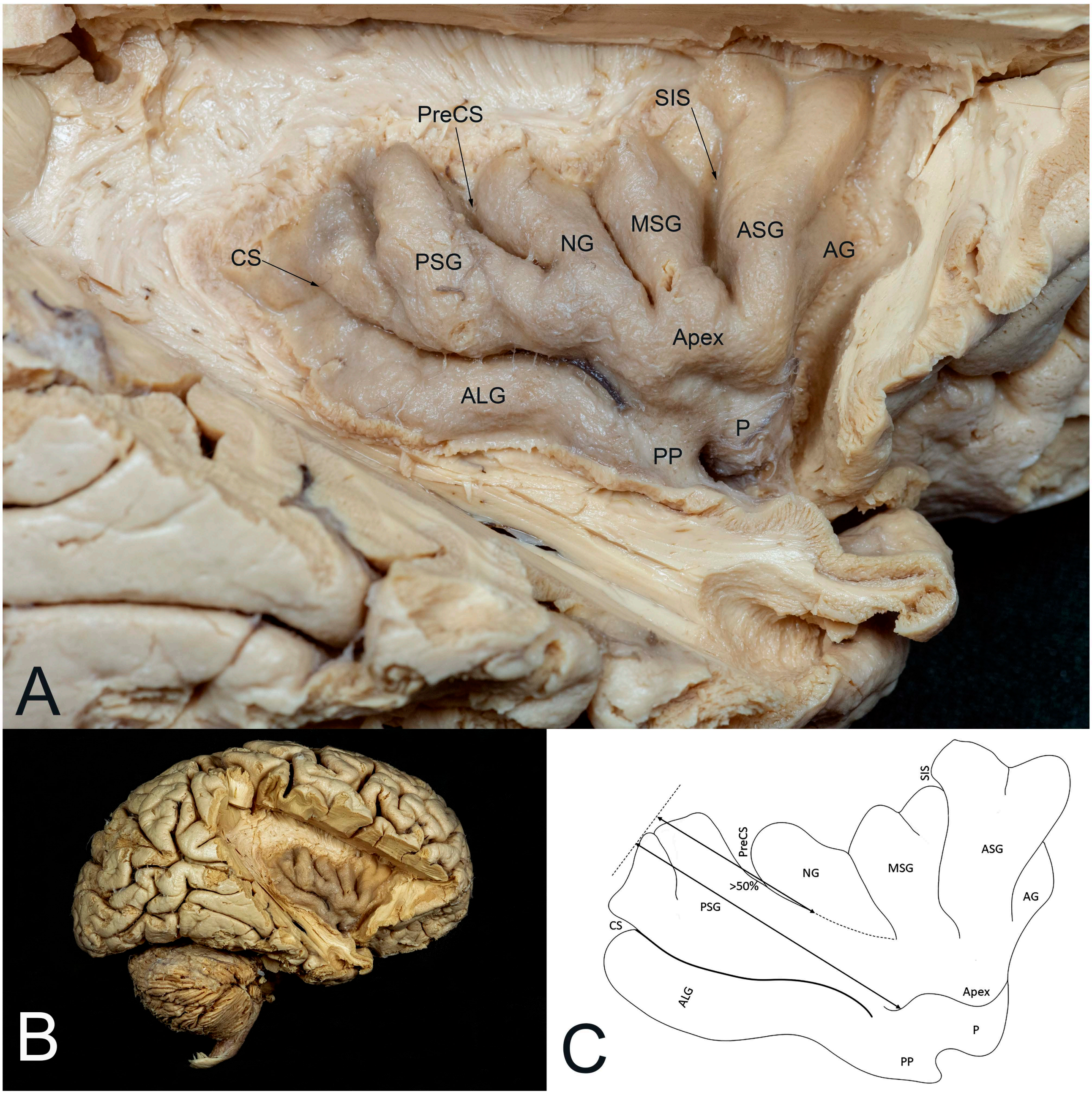

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Table 1 - Paired t-test results on the short gyri length and width comparison

	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; PSG - posterior short gyrus the short insular sulcus (SIS), pre-central insular sulcus (pre-CS) and post-central insular sulcus (post-CS).

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) 4 - 6.7% (4/60) 5 - 61.7% (37/60) 6 - 30% (18/60)	2 - 3.0% (3/60) 3 - 45% (27/60) 4 - 48.3% (29/60) 5 - 1.7% (1/60)	1 - 23.3% (14/60) 2 - 76.7% (46/60)

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)

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

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)

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

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)	

Anexo I

Informação para autores - Clinical Neurology and Neurosurgery

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AUTHOR INFORMATION PACK

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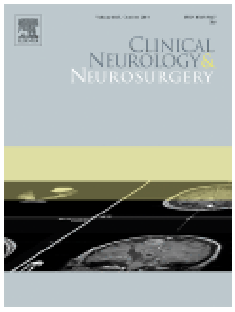

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There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/ book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Formatting requirements
There are no strict formatting requirements but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.
If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.
Divide the article into clearly defined sections.

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Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). See also the section on Electronic artwork.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

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Subdivision - numbered sections

Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Material and methods

Provide sufficient details to allow the work to be reproduced by an independent researcher. Methods that are already published should be summarized, and indicated by a reference. If quoting directly from a previously published method, use quotation marks and also cite the source. Any modifications to existing methods should also be described.

Results

Results should be clear and concise.

Discussion

This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

• ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

• ***Author names and affiliations.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

• ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**

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Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

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List: Number the references (numbers in square brackets) in the list in the order in which they appear in the text.
Examples:
Reference to a journal publication:
[1] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, The art of writing a scientific article, J. Sci. Commun. 163 (2010) 51–59. https://doi.org/10.1016/j.Sc.2010.00372.
Reference to a journal publication with an article number:
[2] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, 2018. The art of writing a scientific article. Heliyon. 19, e00205. https://doi.org/10.1016/j.heliyon.2018.e00205.
Reference to a book:
[3] W. Strunk Jr., E.B. White, The Elements of Style, fourth ed., Longman, New York, 2000.
Reference to a chapter in an edited book:
[4] G.R. Mettam, L.B. Adams, How to prepare an electronic version of your article, in: B.S. Jones, R.Z. Smith (Eds.), Introduction to the Electronic Age, E-Publishing Inc., New York, 2009, pp. 281–304.
Reference to a website:
[5] Cancer Research UK, Cancer statistics reports for the UK. http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/, 2003 (accessed 13 March 2003).
Reference to a dataset:
[dataset] [6] M. Oguro, S. Imahiro, S. Saito, T. Nakashizuka, Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1, 2015. https://doi.org/10.17632/xwj98nb39r.1.

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We will do everything possible to get your article published quickly and accurately. Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will only be considered at this stage with permission from the Editor. It is important to ensure that all corrections are sent back to us in one communication. Please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility.

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Anexo II

Parecer da Comissão de Ética do Centro Hospitalar Universitário de São João/ Faculdade de Medicina da Universidade do Porto

SÃO JOÃO

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

Questionário para submissão de Investigação

*Exmo. Sr. Presidente da Comissão de Ética do Centro Hospitalar de São João/
Faculdade de Medicina da Universidade do Porto,*

Pretendendo realizar a investigação infracitada, solicito a V. Exa., na qualidade de Investigador, a sua apreciação e a elaboração do respetivo parecer. Para o efeito, anexo toda a documentação requerida.

IDENTIFICAÇÃO DO ESTUDO

Título da investigação: Anatomia Neurocirúrgica do Córtex Insular

Nome do investigador: Diogo da Cunha Cabral

Endereço eletrónico: diogo.cabral08@outlook.com **Contacto telefónico:** 968050772

Caracterização da investigação:

☐ Estudo retrospetivo ☒ Estudo observacional ☐ Estudo prospetivo

☐ Inquérito ☐ Outro. Qual? ____

Tipo de investigação:

☐ Com intervenção ☒ Sem intervenção

Formação do investigador em boas práticas clínicas *(GCP)*: ☐ Sim ☒ Não

Promotor *(se aplicável)*: ____

Nome do orientador de dissertação/tese *(se aplicável)*: José Paulo Andrade

Endereço eletrónico: jandrade@med.up.pt

Local/locais onde se realiza a investigação: Unidade de Anatomia do Departamento de Biomedicina da FMUP

Data prevista para início: 20 / 04 / 2019 Data prevista para o término: 27 / 06 / 2019

PROTOCOLO DO ESTUDO

Síntese dos objetivos:

Aprofundamento do conhecimento existente acerca da morfologia do córtex insular, no que diz respeito à organização dos diferentes sulcos e circunvoluções que caracterizam a superfície insular, bem como avaliar quais as variações mais prevalentes.

Fundamentação ética (ganhos em conhecimento/inovação; ponderação benefícios/riscos):

A ínsula é um estrutura localizada profundamente na fissura lateral (de Sylvius) que apresenta importantes funções gustativas, auditivas comportamentais, de linguagem e regulação cardiopulmonar.

A sua localização estratégica junto de determinadas estruturas cerebrais de difícil acesso tornam a ínsula uma possível via de acesso neurocirúrgica a estas mesmas estruturas. Por outro lado, sabe-se hoje que a ínsula poderá estar envolvida em determinadas formas de epilepsia, sendo atualmente um alvo da cirurgia da epilepsia.

Desta forma, pelas razões supramencionadas e pela necessidade de desenvolvimento de técnicas neurocirúrgicas que evitem dano e áreas funcionalmente importantes, torna-se fundamental um conhecimento aprofundado e detalhado da anatomia do córtex insular e da variabilidade que lhe está associada.

CONFIDENCIALIDADE

De que forma é garantida a anonimização dos dados recolhidos de toda a informação?

O investigador necessita ter acesso a dados do processo clínico? ☐ Sim ☐ Não

Está previsto o registo de imagem ou som dos participantes? ☐ Sim ☐ Não

Se sim, está prevista a destruição deste registo após o sua utilização? ☐ Sim ☐ Não

CONSENTI MENTO

O estudo implica recrutamento de:

Doentes: ☐ Sim ☒ Não Voluntários saudáveis: ☐ Sim ☒ Não

Menores de 18 anos: ☐ Sim ☒ Não

Outras pessoas sem capacidade do exercício de autonomia: ☐ Sim ☒ Não

A investigação prevê a obtenção de Consentimento Informado: ☐ Sim ☒ Não

Se não, referir qual o fundamento para a isenção:

Existe informação escrita aos participantes: ☐ Sim ☒ Não

PROPRIEDADE DOS DADOS

A investigação e os seus resultados são propriedade intelectual de:

☒ Investigador ☐ Promotor ☐ Ambos ☐ Serviço onde é realizado

☐ Não aplicável Outro: ____________________

BENEFÍCIOS, RISCOS E CONTRAPARTIDAS PARA OS PARTICIPANTES

Benefícios previsíveis:

Riscos/incómodos previsíveis:

São dadas contrapartidas aos participantes:

- *pela participação* ☐ Sim ☐ Não ☐ Não aplicável
- *pelas deslocações* ☐ Sim ☐ Não ☐ Não aplicável
- *pelas faltas ao emprego* ☐ Sim ☐ Não ☐ Não aplicável
- *por outras perdas e danos* ☐ Sim ☐ Não ☐ Não aplicável

CUSTOS / PLANO FINANCEIRO

Os custos da investigação são suportados por:

☐ Investigador ☐ Promotor ☐ Serviço onde é realizado

☒ Não aplicável Outro: ____________________

Existe protocolo financeiro? ☐ Sim ☒ Não

LISTA DE DOCUMENTOS ANEXOS

- [ ] Pedido de autorização ao Presidente do Conselho de Administração do Centro Hospitalar de São João *(se aplicável)*
- [ ] Pedido de autorização à Diretora da Faculdade de Medicina da Universidade do Porto *(se aplicável)*
- [x] Protocolo do estudo
- [x] Declaração do Diretor de Serviço onde decorre o estudo
  (sendo um estudo na área de enfermagem deve anexar também a concordância da chefia de enfermagem)
- [ ] Profissional de ligação
- [x] Informação dos orientadores
- [ ] Informação ao participante
- [ ] Modelo de consentimento
- [ ] Instrumentos a utilizar *(inquéritos, questionários,escalas, p.ex.)*: ____________
- [x] Curriculum Vitae abreviado *(máx. 3 páginas)*
- [ ] Protocolo financeiro
- [ ] Outros:

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (1960 e respetivas emendas), e da Organização Mundial da Saúde, Convenção de Oviedo e das "Boas Práticas Clínicas" (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CES o relatório final da investigação, assim que concluído.

Porto, 10 *de* março *de* 2019

Nome legível: Diogo da Cunha Cabral — Diogo da Cunha Cabral

assinatura

Parecer da Comissão de Ética do Centro Hospitalar de São João/ FMUP — Emitido na reunião plenária da CE de 12 / 04 / 19

A Comissão de Ética para a Saúde APROVA por unanimidade o parecer do Relator, pelo que nada tem a opor à realização deste projecto de investigação.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

SÃO JOÃO
HOSPITAL

Parecer da Comissão de Ética para a Saúde do
Centro Hospitalar Universitário de São João / Faculdade de Medicina da Universidade do Porto

Título do Projecto: Anatomia Neurocirúrgica do Córtex Insular.

Nome do Investigador Principal: Diogo da Cunha Cabral, aluno do Mestrado Integrado em Medicina da FMUP.

Onde decorre o Estudo: Na Unidade de Anatomia do Departamento de Biomedicina da FMUP. Dispõe de autorização da Prof.ª Doutora Maria Dulce Cordeiro Madeira.

Objectivos do Estudo: Estudo observacional sem intervenção que tem como principal objectivo aprofundar o conhecimento existente acerca da morfologia do córtex insular, no que diz respeito à organização dos diferentes sulcos e circunvoluções que caracterizam a superfície insular, bem como avaliar quais as variações mais prevalentes.
Estudo realizado no âmbito do Mestrado Integrado em Medicina da FMUP, sob orientação do Prof. Doutor José Paulo Alves Vieira de Andrade.

Concepção e Pertinência do estudo: Hemisférios cerebrais pertencentes ao material de estudo da unidade de Anatomia do Departamento de Biomedicina da FMUP, provenientes da doação cadavérica e obtidos no âmbito da colaboração com o INMLCF serão utilizados para caracterização morfológica pormenorizada do córtex insular.

Benefício/risco: Não aplicável.

Confidencialidade dos dados: Não aplicável.

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável.

***Curriculum* do investigador**: Adequado à investigação.

Data previsível da conclusão do estudo: Junho de 2019

Conclusão: Em face a análise do estudo, proponho um parecer favorável à sua realização. A CES sugere que o título do trabalho seja alterado, na medida em que não é um projeto no âmbito da neurocirurgia.

Porto, 12 de Abril de 2019

O Relator da CES, Prof. Manuel Pestana