Epilepsy & Seizure
Journal of Japan Epilepsy Society
Vol. 14 No. 1 (2022) pp.25-33

Mini-Review

The risks of insular and insulo-opercular epilepsy surgery

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Key words: Insular epilepsy; Insular or insulo-opercular resection; Surgical risks; Motor complications

Received: December 31, 2021; Accepted: March 21, 2022

Abstract

Insular or insulo-opercular resection for treating intractable epilepsy represents a significant neurosurgical challenge. Seizure outcomes have improved considerably with the accumulation of knowledge of insular epilepsy in the last decade. However, the surgical risks have not been well documented. In this article, we review the risks of insular or insulo-opercular epilepsy surgery, focusing on the putative roles of the insula, such as sensorimotor function, cognition, and social-emotional function. Insular resection does not cause a significant impairment of cognition, but poses a risk of postoperative motor complications and may affect emotional perception. Insular or insulo-opercular resection is a promising surgical treatment option for intractable epilepsy. However, further research is required to limit complications and improve safety.

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Introduction

The frequency of insular or insulo-opercular epilepsy surgeries has increased because of a deeper pathological understanding and improved diagnostic techniques. Therefore, seizure outcomes have improved, with a complete remission rate of approximately 70% [1]. However, surgeries are difficult to perform because of the complex anatomy and the obscure physiological functions of the insula. Moreover, the surgical risks are poorly understood. In this mini-review, we describe the anatomy and putative roles of the insula required to conduct safe insular or insulo-opercular resection and to identify the risks.

Anatomy

The insula is located deep within the Sylvian fissure and is covered by the frontal, temporal, and parietal lobes. The insula consists of three short and two long gyri and is

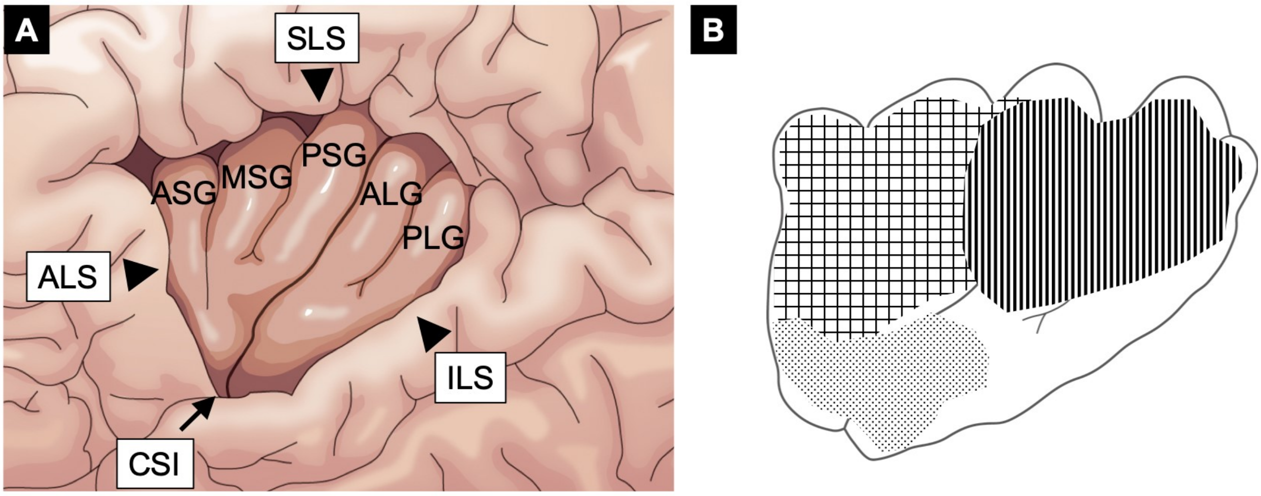

Figure 1 Anatomy of the insula (left lateral view). **A**. Surface anatomy. The insula consists of five gyri: the anterior short gyrus (ASG), middle short gyrus (MSG), posterior short gyrus (PSG), anterior long gyrus (ALG), and posterior short gyrus (PSG). The edge of the insula is defined by three limiting sulci (arrowheads): the superior edge of the superior limiting sulcus (SLS), the anterior edge of the anterior limiting sulcus (ALS), and the inferior edge of the inferior limiting sulcus (ILS). The central sulcus of the insula (CSI) is the most prominent sulcus between the PSG and ALG and separates the anterior and posterior insula (arrow). **B**. Functional anatomy by Kurth et al. [3]. Grid: cognition, stripe: sensorimotor function, dot: social-emotional function.

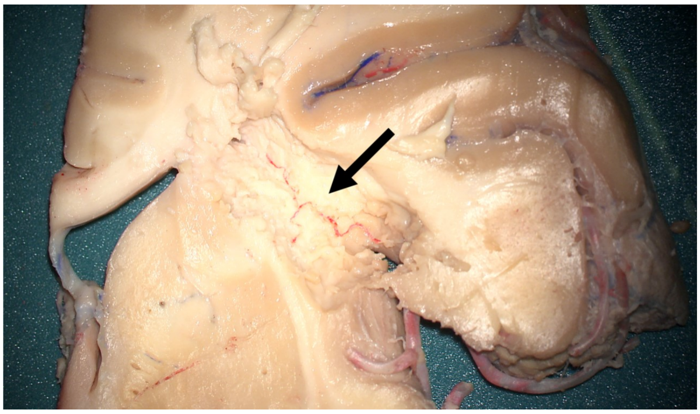

Figure 2 A cadaveric image of the long insular artery on coronal section. LIA, a small perforator-like artery, penetrates the brain in the vicinity of the superior limiting sulcus and terminates in the deep white matter close to the lateral ventricle (arrow).

surrounded by three limiting sulci. The central sulcus of the insula separates the short and long gyri and serves as a landmark for the boundary between the anterior and posterior insula (Fig. 1A).

The blood flow to the insula is supplied by the middle cerebral artery (MCA) alone. The MCA is divided into four segments: M1, the first segment; M2, the second segment that runs on the insular cortex; M3, the third segment on the operculum; and M4, the last segment after exiting the Sylvian fissure. The lenticulostriate artery (LSA) is a perforating artery that arises mainly from the M1 segment and reaches the posterior limb of the internal capsule. The long insular artery (LIA) is a perforator-like small artery, which arises from M2 and M3 and reaches the corona radiata. In this study, the LSAs and LIAs will be described in detail, with special emphasis on the context of surgical risks.

Putative roles of the insula and surgical risks

Recent studies have shown that the insula is involved in interoception, somatosensory sensations, articulation, motor function, hearing, vestibular function, autonomic function, emotion, behavior, and cognition [1-7]. Moreover, these functions are seemingly derived from the brain regions surrounding the insula.

Kurth et al. [3] classified the insular cortex into three functional regions (Fig. 1B):

Sensorimotor function – posterior insula.

Cognition – anterior insula, involved in attention, language, speech, working memory, and memory

Social-emotional function – anteroinferior insula

Based on these locations, we primarily focused on the evidence from surgical cases, because results from activation studies may differ from those based on resections (Table 1).

Sensorimotor function

Postoperative permanent motor paralysis occurs in approximately 5% of insular and insulo-opercular surgeries [8]. The risk of motor paralysis after insular and insulo-opercular surgeries was first documented in patients with brain tumors and vascular diseases [7, 9-11]. Preservation of critical arteries, including the M2, M3, and M4 branches of the MCA and LSAs, is crucial because postoperative ischemia is a major cause of motor complications [12]. To preserve the LSAs, the most lateral branch of the LSAs penetrating the brain should first be observed during surgery. Thereafter, using this artery as a guide, the deepest part of the resection should be determined—this helps avoid ischemia of the corticospinal tract [7]. In epilepsy surgery, the same extent of resection can be achieved by limiting the resection to the extreme capsule.

Posterior insular resection is another risk factor for postoperative motor complications [11], and damage to LIAs is the most probable cause of this complication. LIAs are small arteries that appear as perforators or with intermediate size—between that of the perforators and medullary arteries. They account for 3–5% of the insular arteries [13]. Additionally, LIAs are the most abundant in the posterior insula. Recent studies have shown that LIAs branch from M2 or M3 penetrate the brain

Table 1 Effects of insular and insulo-opercular surgery

Authors	Reference	No. of pts	Tests / Evaluation Items	Observations (Effect of insular and insulo-opercular surgery)
Cognition				
Boucher et al. (2015)	[19]	18	WAIS-III, TMT-A/-B, STROOP-C/-W/-I, AVLT, RCFT, BNT, VF	Significant worsening of color naming speed in STROOP-C → depending on oro-motor speed rather than cognitive impairment
Freri et al. (2017)	[21]	16	cognitive function (unknown)	Improved in 38% cases, no change in 62% cases
Mullatti et al. (2019)	[22]	19	neuropsychological status (unknown)	Improved or no change
Ikegaya et al. (2020)	[20]	15	WISC-III or -IV, T-B test, KIDS	No significant change in IQ and DQ
Sociality and emotion				
Boucher et al. (2015)	[24]	15	ERT, Reading the Mind in the eyes test, Interpersonal Reactivity Index	Change in emotional recognition, such as happiness, surprise, and fear
Citherlet et al. (2020)	[26]	16	Emotional Stroop test, Dot-Probe test	Altering emotional interference control
Gravel et al. (2021)	[27]	27	BDI-II, STAI-T, QOLIE-10-P	No significant change in the scores of depression, anxiety, and quality of life
Others				
Von Siebenthal et al. (2016)	[28]	26	IGT, Cups Task	Risky decision making when facing a potential loss
Hébert-Seropian et al. (2017)	[29]	19	ISPC	Mild but significant increases in irritability, emotional lability, anxiety, and frugality
Lacuey et al. (2019)	[30]	21	HRV	Decrease in heart rate (autonomic dysfunction)
Hébert-Seropian et al. (2021)	[31]	17	CEHEQ	Decrease in appetite (59%)

Abbreviations: Pts, patients; WAIS-III, Wechsler Adult Intelligence Scales, Third Version; TMT-A/-B, Trail Making Test Parts-A, -B; STROOP-C/-W/-I, Stroop Test -Color Naming, -Word Reading, -Interference; AVLT, Auditory Verbal Learning Test; RCFT, Rey-Osterrieth Complex Figure Test; BNT, Boston Naming Test; VF, Verbal Fluency test; WISC, Wechsler Intelligence Scale for Children; T-B test, Tanaka-Binet test; KIDS, Kinder Infant Development Scale; IQ, intelligence quotient; DQ, developmental quotient; ERT, Emotion recognition task; BDI-II, Beck Depression Inventory, 2nd edition; STAI-T, State-Trait Anxiety Inventory, Trait Version; QOLIE-10-P, Patient Weighted Quality of Life in Epilepsy; IGT, the Iowa Gambling Task; ISPC, the Iowa Scales of Personality Change; HRV, heart rate variability; CEHEQ, Changes in Eating Habits and Experiences Questionnaire

adjacent to the superior limiting sulcus and terminate in the corona radiata (Fig. 2) [14, 15]. Thus, LIA injury may manifest characteristic image finding of ischemic changes extending to the corona radiata (Fig. 3). Moreover, this ischemia is found in 55% of all insular resections, including anterior surgeries [16]. In these cases, ischemia extending to the corticospinal tract (CST; located below the posterior insula) can induce motor complications. This may explain why LIA injuries often lead to transient hemiparesis

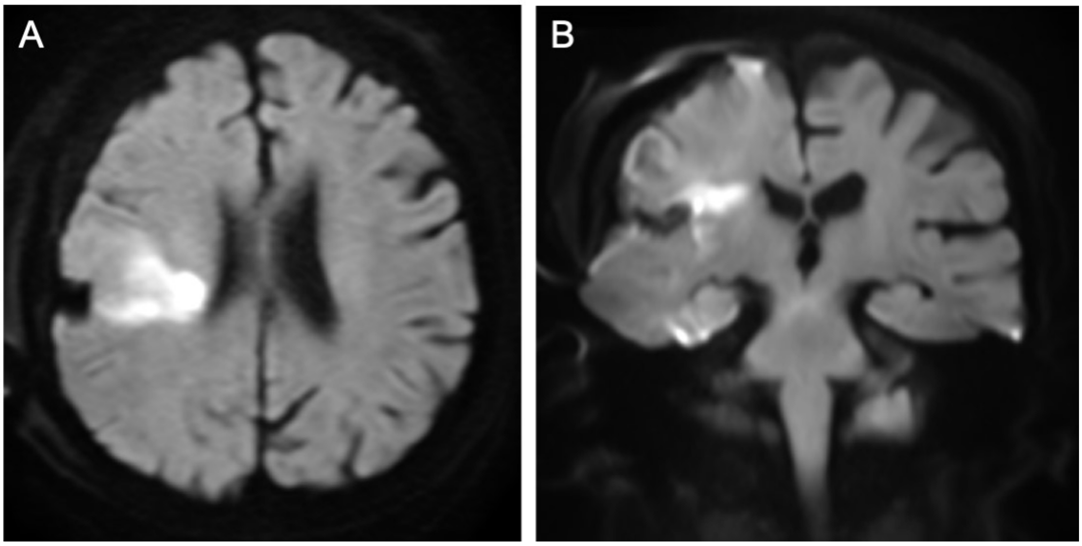

Figure 3 A representative case of ischemic motor complication due to long insular artery injury. The trans-opercular approach was used to resect the opercular glioma located in the vicinity of the superior limiting sulcus (SLS) in this case. Postoperative diffusion-weighted images (A: axial; B: coronal) show ischemic changes from SLS to the corticospinal tract, suggesting injury to the LIA at the SLS. The patient developed mild hemiparesis that was still present eight months after surgery.

and why the incidence of permanent complications caused by LIA injuries is lower than that caused by LSA injuries.

Another possible mechanism of motor complication is cortical resection. Bouthillier et al. [17] reported that frontal opercular resection was significantly associated with motor deficits. They proposed that these deficits were dual or multifactorial, i.e. loss of cortical function from the opercular resection itself, retraction of the opercula, and/or subsequent ischemia at the CST. However, this finding could also be interpreted as evidence that the long medullary arteries (LMAs) from the opercula can cause motor complications. Indeed, Bouthillier et al. also indicated that frontal opercular resection was a significant predictor of postoperative radiological ischemic changes in the corona radiata. In support of this observation, another study demonstrated that LMA can distribute to the corona radiata and cause ischemic motor complications [10] Therefore, opercular resection may contribute to motor complications by causing ischemia in the LMA. Thus, these complications may be similar to those caused by insular resection and LIA ischemia.

Two techniques have been proposed to avoid these motor complications. The first approach involves the use of motor evoked potential (MEP). Continuous MEP monitoring is essential. In addition, identification and temporary occlusion of the LIA under MEP monitoring may aid in avoiding ischemic complications, but identification is technically difficult [18]. The second approach involves the preservation of a small piece of gray matter at the upper part of the insula [8]. These techniques are promising to avoid damage to the LIA feeding the corona radiata, but require validation in further studies.

Cognition

Current research indicates no major changes in cognition after insular or insulo-opercular epilepsy surgery, although cognitive tasks such as attention, working memory, language, and visuospatial function activate the insula [19, 20]. Verbal and visual memory also show no decline in adult cases of insular or insulo-opercular epilepsy surgery, but no research has been done on pediatric cases due to the complexity of the cognitive tests. A previous study demonstrated a decrease in color naming speed using the Stroop test [19]. However, this depends on oro-motor speed rather than cognitive function. Another study implied that poor seizure outcome, rather than resection, may impact cognitive decline in some cases [20]. Surprisingly, cognitive function may improve after insular surgery [21, 22]. Further clinical studies are needed to verify this positive effect.

Emotion and sociality

Emotional recognition through facial expression may be an insular function. The recognition of disgust has received special attention as a specific function of the insula [23], but recent studies have shown that insular resection can also impair the recognition of happiness, surprise, and fear [24, 25]. This suggests that insular damage leads to poor emotional sensitivity across emotions. Another study showed that insular resection may cause cognitive conflict [26]. Moreover, a self-reported empathy questionnaire revealed that perspective taking is more difficult in patients who underwent insular surgery than in healthy controls [24]. These results suggest that insular resection can affect recognition or processing of emotions, and empathy.

Depression and anxiety after insular surgery were not particularly common compared to temporal lobe epilepsy surgery, although the scores of depression and anxiety were higher among people with epilepsy [27]. Thus, the risks of psychological issues after insular surgery may not be significant compared to other epilepsy surgeries.

Other risks

Patients who underwent resection of the insula tended to make rash gambling decisions compared to healthy controls [28]. This indicates that the insula is involved in decision-making. Subtle but significant changes in irritability, emotional lability, and frugality were observed after insular resection [29]. Moreover, recent studies suggest that insular resection may alter the autonomic function and decrease appetite [30, 31]. Further studies are needed to elucidate the relationship between resections and serious outcomes due to autonomic failure, such as sudden unexpected death in epilepsy, and eating disorders due to appetite loss.

Perspective

Motor complications are increasingly recognized as complications of insular and insulo-opercular surgery, but this relationship is not fully understood. Detailed anatomical and clinical studies are lacking—for example, studies on arterial supply from the vicinity of the superior limiting sulcus, including the LIA and LMA. Further studies are needed to establish safe surgeries to limit motor complications after insular and insulo-opercular surgery.

Cognition and social-emotional function may be affected after insular resection, but the current evidence in support of this finding is insufficient. Moreover, some insular functions have not been evaluated fully, such as social and socio-psychological behavior. This evaluation will require multidisciplinary collaboration with clinical psychologists and higher brain function specialists. In addition, to better understand the effects of insular surgery on psychological and sociopsychological behaviors, larger long-term cohort studies are required. Establishing an international registry is a possible solution to address these issues.

Conclusion

This article reviews the surgical risks associated with insular and insulo-opercular resections. Insular resection does not cause a significant decrease in cognition, but it poses a risk of postoperative motor complications and may affect emotional perception.

Acknowledgements

We thank Dr. Jun Suenaga for providing the brain images used in Figure 2. This work was conducted by the Publication Task Force of the Japan Young Epilepsy Section (YES-Japan), which is a national chapter of The Young Epilepsy Section of the International League Against Epilepsy (ILAE-YES).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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