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Neuropsychological performance before and after partial or complete insulectomy in patients with epilepsy

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ABSTRACT

Resection of the insular cortex is becoming more frequent as it is increasingly recognized that a nonnegligible proportion of surgical candidates with drug-resistant epilepsy have an epileptogenic zone that involves the insula. In the last decades, however, the insula has been proposed to be involved in several neuropsychological functions, and there is a lack of documentation on whether partial or complete insulectomy results in permanent cognitive impairments in this clinical population. In this study, we conducted standard preoperative and postoperative neuropsychological assessments in 18 patients undergoing epilepsy surgery that included the removal of the insula in the right ($n = 13$) or the left ($n = 5$) hemisphere. Postoperative testing was conducted at least five months after surgery. Cognitive impairments were common and heterogeneous prior to surgery, with language and verbal memory impairments being especially frequent among patients in whom epileptic seizures originated from the left hemisphere. After surgery, declines and improvements occurred on a variety of outcomes, although new deficits were relatively infrequent among patients who had obtained normal performance at baseline. Statistical comparisons between preoperative and postoperative assessments revealed significant deterioration of only one outcome – the color naming condition of the Stroop test – which relies on oro-motor speed and lexical access. These findings suggest that partial or complete resection of the insular cortex in patients with drug-refractory epilepsy can be conducted without major permanent neuropsychological impairments in a vast majority of patients. However, small decrements in specific cognitive functions can be expected, which should also be taken into account when considering the surgical option in this clinical population.

1. Introduction

The insula, considered as the fifth lobe of the human brain, is located deep in the sylvian fissure, hidden behind the frontal, temporal, and parietal opercula. Work from our group and that from others have shown that a nonnegligible proportion of surgical candidates with drug-resistant epilepsy have an epileptogenic zone that involves the insula [1–4] and that failure to recognize it may be responsible for epilepsy surgery failures [5,6]. Consequently, an increasing number of insular resections have been reported for epilepsy control purposes [4,7–9].

The role of the insular lobe in visceral and sensory functions is well established and has been demonstrated by various methods including direct electrical stimulation of the cortex [3,5,10,11]. However, its contribution to cognitive functioning has long remained enigmatic and is still controversial, although our understanding has benefited greatly from recent clinical and functional neuroimaging studies [12–14]. Notably, the insula has been associated with language [15,16], verbal memory [17], attention [18,19], and other higher-order executive processes [20,21]. Whether partial or complete resection of the insula for treatment of drug-refractory epilepsy affects these cognitive functions and whether either resection results in clinically significant neuropsychological impairments remain poorly documented.

Effects of insular resection on cognitive function have been described in patients who underwent neurosurgery for resection of insular tumors. Common deficits reported immediately following surgery include aphasia and hemiparesis, and other symptoms such as lethargy and "slowness of ideation" have also been described [22–26]. Fortunately, in most cases, these impairments appeared to be transient, improving or disappearing completely within 3 months, suggesting that resection of the insular cortex can be accomplished without producing devastating functional deficits. However, most reports relied solely on follow-up neurological examination and did not include a standard, extensive neuropsychological assessment, which could help in identifying subtle and specific cognitive impairments. To our knowledge, only one

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study has assessed the performance of a group of patients prior to and three months after the resection of Grade II or III insular gliomas, using a comprehensive battery of neuropsychological tests [27]. Decline in performance was observed on a variety of outcomes and somewhat more specifically for verbal learning. However, results were heterogeneous across patients, and the nature of the postoperative cognitive deficits was found to be largely determined by the side of the tumor.

In the present study, we examined the effect of epilepsy surgeries which comprised partial or complete removal of the insular cortex on neuropsychological function.

2. Material and methods

2.1. Participants

Our sample includes all adult patients ($N = 18$) who underwent partial or complete insular resection for control of drug-resistant epilepsy in our epilepsy service, during the period extending from October 2000 to July 2013, for whom neuropsychological assessments were conducted both before and after surgeries. The decision to operate and site of surgery were based on a complete epilepsy workup, including video-electroencephalographic monitoring, MR imaging, ictal single-photon emission computed tomography, positron emission tomography, magnetoencephalography, and, when necessary, intracranial electroencephalographic recordings. Language dominance was determined by one or more approaches: functional near-infrared spectroscopy, functional magnetic resonance imaging, intracarotid amobarbital test, and/or cortical stimulation. Presurgical investigation details for some of these patients, as well as operative techniques, have been described elsewhere [3,8,28].

Patient characteristics and information about surgery are presented in Table 1. All but two patients were right-handed. All patients were left-hemisphere dominant, with the exception of one (patient 14) who had bilateral representation of language. Interictal scalp EEG allowed correct classification of the hemisphere of seizures in all but one case. Magnetic resonance imaging revealed no obvious epileptogenic lesion in ten patients and revealed focal cortical dysplasia in four patients, hippocampal sclerosis in two patients, several tubers in one patient with tuberous sclerosis, and a congenital encephalomalacic lesion in the right frontal lobe in one patient.

Surgeries were performed in the right hemisphere for 13 patients and in the left hemisphere for the remaining five patients. Only one patient had a pure insulectomy. The remaining insulectomies were combined with an opercular resection in twelve patients [two of which had a prior unsuccessful resection within the frontal lobe (patients 17 and 18) and one in the parietal operculum (patient 11)], a temporal lobectomy in four patients, and a frontal lobectomy in one patient. The extent of insular resection varied between subjects: radical insulectomy was performed in three cases; partial resection confined to the anterior insula was conducted in nine patients, to the posterior insula in four patients, and to the inferior insula in two cases. Overlapping areas of resection and postsurgery MRI scans from representative cases of the study sample are depicted in Fig. 1. Small ischemic infarcts related to injury of perforating branches (mainly of M2, rarely M3 or M4 segments) of the middle cerebral artery during insulectomies (typically located in the corona radiata running from the insula to the periventricular region) were found on postoperative MRI in eleven (61%) subjects. Five (28%) patients experienced contralateral paresis, which was transient in four of them, and three experienced transient aphasia (17% of all surgeries; 60% of left-hemisphere surgeries). One patient had hypoesthesia of the left arm and cheek most likely related to the resection of the inferior postcentral gyrus rather than the posterior third of the insula.

2.2. Neuropsychological assessment

Only the neuropsychological tests for which most participants had available data at both preoperative and postoperative assessments were selected for the scope of this study. The list of test abbreviations with domains assessed is presented in Table 2.

Three tests were used to assess attention and executive functions. In the Digit-Symbol (SYMB) subtest of the Wechsler Adult Intelligence Scales — Third Version [29], digit symbol associations are illustrated at the top of the page. Under each digit, the participant must write the matching symbol within a limited period of 2 min. The Trail Making Test is a well-established measure of visual attention and mental flexibility [30]. In Part A (TMT-A), the participant is shown a sheet with circled numbers and is asked to draw a line connecting the circles in ascending numerical order as fast as possible. In Part B (TMT-B), numbers are mixed with letters, and the participant must connect the circles by switching between numbers and letters, following numerical and alphabetic orders. The Stroop Color-Word Test assesses oro-motor speed and interference inhibition and comprises three conditions. In Color Naming (STROOP-C), the participant is required to name the ink color of small rectangles presented on a sheet as quickly as possible. In Word Reading (STROOP-W), words denoting colors are presented, and the participant is asked to read them aloud as fast as he or she can. In the Interference condition (STROOP-I), color words are presented with dissonant ink color, and the participant is asked to name the ink color as quickly as possible. Most patients ($n = 10$) were assessed with the version of the task included in the Delis–Kaplan Executive Function System [31] at both assessments, and five were assessed with a four-color version of the Stroop test [32,33] on at least one occasion.

Working memory was assessed with the Digit Span (SPAN) test [29]. The examiner first reads sequences of numbers to the participant, who is asked to repeat them in the order presented. Sequences lengthen until the participant fails two consecutive trials of the same length. Then, the participant is asked to recall new sequences in reverse order.

Verbal memory was assessed using the Rey Auditory Verbal Learning Test [34,35]. A first 15-word list is presented orally to the participant, who has to recall as many words as possible in any order during five successive learning trials (AVLT-L). An immediate recall trial of this list is performed after the presentation of an interfering list, and a delayed recall trial is performed 20 min later (AVLT-D). In order to minimize practice effects, parallel forms with different word lists were used at the preoperative and postoperative assessments.

Visual memory was assessed using the Rey Complex Figure Test and Recognition Trial [36]. The participant is first asked to copy a complex figure on a blank sheet. Immediate and delayed reproduction trials are performed three and 30 min after the initial copy, respectively. The delayed reproduction (RCFT-DR) is followed by a recognition trial (RCFT-REC) in which the participant is presented a series of designs and must indicate whether each design was part of the initial figure or not. The traditional Rey–Osterrieth figure was used at each assessment.

Language was assessed using three different tasks. The Boston Naming Test (BNT) was used to assess picture-naming abilities [37]. In this task, the participant is asked to name a series of pictures of living or nonliving objects. Semantic and phonologic cueing is provided when the participant is unable to name the object spontaneously. In the verbal fluency task, participants were asked to generate as many words as possible in 60 s [31]. Three trials of letter fluency (VF-LETT) and two trials of category fluency (VF-CATEG) were performed. In the Similarities subtests (SIM) [29], pairs of words are presented to the participant, who is asked to indicate how the words relate semantically. This latter task requires verbal abstraction.

Visuoconstruction was assessed using the Block Design (BLOCK) test [29]. In this task, the participant is asked to reproduce illustrated designs using cube-shaped blocks within a given time period.

All assessments were conducted or supervised by a skilled, licensed neuropsychologist, before and at least five months after neurosurgery, with the patient's informed consent. Two patients were assessed in English because they were native English speakers; the others were tested in French.