

Neglect After Right Insular Cortex Infarction

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Background and Purpose—Case reports have shown an association between right insular damage and neglect. The aim of this study was to examine the incidence of neglect among patient groups with right or left insular infarction.

Methods—We examined neglect in 9 right-handed subjects with insular stroke as evidenced by CT and/or MRI scans (4 with right insular and 5 with left insular cerebrovascular accident) between 4 and 8 weeks after acute stroke with tests of visual, tactile, and auditory perception.

Results—Compared with patients with left insular lesions, patients with right insular lesions showed significant neglect in the tactile, auditory, and visual modalities.

Conclusions—The right insular cortex seems to have a role in awareness of external stimuli, and infarction in this area may lead to neglect in multisensory modalities. (*Stroke*. 1999;30:946-948.)

Key Words: cerebral cortex ■ cerebral infarction ■ hemineglect ■ insula

Neglect is the failure to report, respond, or orient to meaningful or novel stimuli.¹ This failure is not accounted for by sensory or motor deficits and primarily occurs in response to stimuli or actions that occur on the side contralateral to a hemispheric lesion. Neglect is most commonly associated with lesions in the right inferior parietal lobe^{1,2} although other areas, including the dorsolateral frontal lobe,³ the thalamus, and the mesencephalic reticular formation⁴ have also been reported to produce neglect in humans.

The human insular cortex is an island of cortical tissue beneath the frontoparietal and temporal opercula⁵ that phylogenetically is considered paralimbic cortex.⁶ Because of its connections with limbic and sensorimotor cortices, the insular cortex is believed to play a role in affective and attentional aspects of human behavior. Paralimbic insular regions have functional specialization for behaviors requiring integration between extrapersonal stimuli and the internal milieu.⁷ Based on these connections, one might expect that lesions of the insular cortex may result in disorders of neglect. This was recently observed in a right-handed individual who developed severe multimodal neglect after injury to the right insula, adjacent white matter, and the inner face of the overlying operculum.⁸

In the present study, we investigated the incidence of neglect in 3 sensory modalities in patients with isolated insular infarctions.

Subjects and Methods

Subjects

From among 330 patients admitted for treatment after an acute cerebral infarction, we found 12 patients with isolated insular

infarcts. Of the 12 patients with isolated insular infarcts, we excluded 2 patients with left insular lesion who had aphasia and 1 with a right insular lesion who had a recurrent stroke. For this study we included 4 patients with right insular and 5 with left insular infarcts. All patients were right-handed on the Edinburgh Handedness Inventory.⁹

There were no significant differences between the left and right insular groups in age, time elapsed since stroke, race, education, sex distribution, clinical severity as measured by the NIH Stroke scale,¹⁰ and cognitive impairment as measured by the Mini-Mental State Examination (MMSE). The MMSE¹¹ is an 11-task examination that has been found to be reliable and valid in assessing a limited range of cognitive functions in stroke patients¹²; scores may range from 0 to 30, with a score of ≤ 23 indicative of significant cognitive impairment.

After obtaining their informed consent, we examined 9 right-handed, white patients. Although the patients were predominantly male, 1 patient in the left and 1 patient in the right insular group were female. The mean age was 68 ± 8.5 years for the left insular group and 68 ± 7.2 years for the right insular group. The mean years of education for both groups was 11. The mean time since stroke was 60 ± 7.9 days in the left insular group and 59 ± 3.6 days in the right insular group. The population was primarily composed of patients in Hollingshead classes III and IV.¹³ All patients were free of a personal or family history of psychiatric disorders. The mean MMSE score was 26.8 ± 1.1 for the right insular group and 26.7 ± 1.1 for the left insular group.

Neurological Findings and Neuroradiological Evaluation

Each group showed similar frequencies of motor, sensory, and visual field deficits. The NIH Stroke Scale summary scores were 6.0 ± 2.6 SD for the left lesion group and 9.2 ± 5.3 SD for the right (difference: NS).

Patients were included if they had a single lesion demonstrated by CT and/or MRI scan, with at least 90% or more of the lesion restricted to the insular cortex. CT and/or MRI were performed approximately 2 weeks after the stroke. All scans were indepen-

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dently read by a neurologist (F.M.) and a psychiatrist with experience in neuroimaging (S.P.), who were blinded to results of the neuropsychological examination. All lesion locations were determined and transposed onto templates according to the procedure described by Levine and Grek.¹⁴ For patients included in the study, there was 100% agreement between the 2 readers on lesion location.

Neglect Measures

The double simultaneous stimulation test was used to assess the presence of extinction (failure to notice stimuli on the right or left sides when simultaneously stimulated from both sides). In the tactile domain, the testing was done using 10 double-simultaneous stimulations of finger touch in the dorsum of the hand intermixed with 20 single (10 on each side) in a counterbalanced order.¹⁵ On visual testing, the stimulation was done by wiggling fingers in both visual fields. The subject was requested to respond by pointing with a finger to the side or sides stimulated. In the case of hemianoptic patients, the double-simultaneous stimulation was administered within the normal visual hemifield. In similar fashion, the patients received auditory stimuli. The score was the number correct out of a total of 10.

Visual neglect was also assessed with the line bisection task,¹⁶ a standard clinical test for the detection of unilateral visual neglect. The subject marks the midpoint of 18 staggered lines of 20-mm, 40-mm, and 60-mm lengths. In left neglect the patients typically displace their mark to the right of the objective midpoint, neglecting part of the left of the line. The distance between the left edge of each line and the patient's mark showing the subjective midpoint was measured to the closest millimeter.

Statistical Analysis

Patient groups were compared using Student *t* tests. For discrete variables, we used the Fisher exact test.

Results

Patients with right insular lesions showed greater extinction to bilateral simultaneous stimulation in the tactile modality ($t_{5,5}=7$, $P<0.0008$). In patients with left damage, 4 of 5 showed perfect performance (score of 10) in the tactile modality of the double simultaneous stimulation test, and 1 patient had a close-to-perfect score (9). All patients with right insular infarction showed weaker performance in this test (scores of 2, 3, 1, and 7).

Patients with right insular lesions also showed extinction to double simultaneous stimulation in the auditory modality (scores of 3, 2, 4, and 5) compared with patients with left insular lesion (10, 10, 8, 10, and 7). This difference also reached statistical significance ($t_{3,4}=7$, $P<0.01$). Patients with right insular lesions showed extinction to double simultaneous stimulation in the visual modality, but this difference did not reach statistical significance ($t_{1,7}=7$, $P<0.1$).

On the line bisection tasks, right insular damage patients showed poorer performance in determining the true midpoint than left lesion patients for 60-mm lines ($t_{5,9}=7$, $P<0.0006$) and for 40-mm lines ($t_{2,7}=7$, $P<0.02$) but not for 20-mm lines (Table 1).

Discussion

Our study showed greater severity of somesthetic, audition, and visual neglect among patients with right compared with left insular damage. These findings are consistent with anatomic connections that have been identified between insular cortex and various cortical regions from animal studies.^{7,17,18} The present findings also provide empirical

Neglect Findings in Study Subjects

Test	Left Insula†	Right Insula†
DSS visual left	9.8±1.3	6±1.5
DSS visual right	9.6±.4	9.2±.4
DSS visual both	9.4±.3	8.5±.3
DSS auditory left	9.3±0.8	9.2±0.7
DSS auditory right	10	10
DSS auditory both*	8.4±.9	3.5±1
DSS somesthetic left	10	6.2±1.4
DSS somesthetic right	10	9.7±.1
DSS somesthetic both*	9.8±0.7	3.2±.8
LBT 20	9.8±.3	10.8±.3
LBT 40*	19.6±.5	21.8±.5
LBT 60*	29.3±.4	33.3±.5

DSS indicates double simultaneous stimulation; LBT, line bisection test.

* $P<0.05$. †Values are given in mean±SD millimeters from left.

support for observations of neglect associated with right insular infarction reported in previous case studies.⁸

Scant information is available about the role of the human insular cortex in cognitive processes. Altered behavior following insular damage in humans has previously been described in case reports. Associations between right insula damage and neglect⁸ and left insular damage and aphasia^{19,20} have also been reported. Berthier et al⁸ reported the case of a right-handed patient who, after an ischemic infarction that involved the entire right insular cortex and adjacent white matter, developed a severe neglect syndrome, oral apraxia, mutism, and ideomotor apraxia for the right hand.

Although the presence of neglect is usually considered a sign of parietal lobe dysfunction, it should not be surprising to find neglect in association with nonparietal lesions. A review of neglect syndromes in monkeys and humans suggests that several regions provide an integrated network for the mediation of directed attention.² The 3 cortical components of this network are the posterior parietal lobe, frontal eye fields, and the cingulate gyrus. Heilman et al²¹ have described a neuro-anatomic system involving cortical-limbic-thalamic-reticular components that lead to preparatory activation or arousal toward meaningful stimuli in the contralateral hemisphere. In humans, neglect is most commonly associated with lesions that involve the right inferior parietal lobe, which includes Brodmann's areas 40 and 39. However, there are other areas where lesions in humans have been reported to induce neglect, including the dorsolateral frontal lobes, the mesial frontal lobes including the cingulate gyrus, and the thalamic and mesencephalic reticular formation.¹ Moreover, several reports have clearly shown that lesions elsewhere in the right hemisphere may result in neglect.^{22,23}

Although clinical descriptions of cases with restricted insular lesions are rare, insular anatomy, connectivity, and physiology have been extensively studied in monkeys and humans. The insula sends neural efferents to cortical areas, from which it receives reciprocal afferent projections. Considering both afferents and efferents, the insula has connections with principal sensory areas in the olfactory, gustatory, somesthetic (SI and SII), and auditory (AI and AII) modali-

ties as well as the paramotor cortex (area 6 and perhaps MII), polymodal association cortex, and a wide range of paralimbic areas in the orbital, temporopolar, and cingulate areas.

Most of the insula, especially its anteroventral portion, has extensive interconnections with limbic structures. Through its connections with the amygdala, the insula provides a pathway for somatosensory, auditory, gustatory, olfactory, and visceral sensations to reach the limbic system.¹⁸

It should also be noted that the insular cortex has reciprocal connections with the anterior inferior parietal cortex,²⁴ which produces classical parietal neglect when damaged. On the basis of the above data and anatomic connections, the present finding might be construed to indicate that insular lesions probably disrupt connections with areas that are normally involved in arousal, attention, and activation. Right insular damage, similar to right parietal lobe damage, may impair awareness of external stimuli and lead to neglect.

A limitation of this study should be acknowledged. The number of patients with localized insular lesions was limited and therefore more subtle neglect correlates may have been missed because of a lack of statistical power. However, this is the first group study of neglect that has been conducted in patients with isolated insula damage.

In conclusion, these findings suggest that the insular cortex, because of its anatomic connections, is integrally related to perceptual attention. Damage to the right insular cortex may play a critical role in the development of neglect by disrupting connections between sensory cortices and the limbic system.

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