Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.6878-20
Intern Med 61: 541-546, 2022
http://internmed.jp

【 CASE REPORT 】

A Patient with a Unilateral Insular Lesion Showing Bilaterally Reduced Perception of Noxious Stimulation

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Abstract:

No study has reported a unilateral localized cerebral lesion of the posterior insula bilaterally reducing noxious stimuli perception. A 57-year-old man with an infarct involving the right posterior insula presented with reduced somatosensory response in the upper and lower left extremities. Furthermore, there was a reduced response to noxious stimulation in the right upper and lower limbs. We noted reductions in pain, noxious heat and cold perceptions, and sensitivity to increasing temperature. Other somatic sensations, including non-noxious temperatures, remained intact in the right upper and lower extremities. These findings in our patient with a unilateral insular lesion indicated a bilaterally reduced perception of noxious stimulation.

Key words: insula, infarction, noxious stimulus, bilateral deficit

(Intern Med 61: 541-546, 2022)
(DOI: 10.2169/internalmedicine.6878-20)

Introduction

Studies on local brain damage have demonstrated that the posterior insula is crucially involved in perceiving noxious stimuli, including pain, noxious heat, and noxious cold (1, 2). Studies using functional magnetic resonance imaging have shown that noxious stimulation bilaterally activates the posterior insula (3). Bilateral reduction in the perception of noxious stimuli can be achieved by cortical electrical stimulation of the unilateral posterior insula (4) and deep continuous theta-burst stimulation (5). Given the aforementioned findings, a localized brain lesion involving the unilateral posterior insula might bilaterally reduce the perception of noxious stimuli. However, to our knowledge, there has been no report of such a case.

Veldhuijzen et al. (2) described cases of bilaterally reduced temperature sensation caused by damage involving the unilateral insula. However, in these cases, non-noxious temperature sensation, i.e. the perception of warmth and coldness, was reduced on the same side as the lesion, with pain and noxious temperature sensation on the same side as the lesion being maintained.

We herein report a case of a bilaterally reduced response to noxious stimuli after an infarction involving the right posterior insula.

Case Report

A 57-year-old right-handed man with a history of high blood pressure and hyperglyceridemia was admitted after developing mild left hemiplegia and dysarthria. On admission, magnetic resonance (MR) diffusion-weighted imaging revealed infarction in the upper portion of the right posterior insula, precentral gyrus, postcentral gyrus, and supramarginal gyrus, as well as the white matter beneath these structures (Figure a). MR angiography failed to visualize the right internal carotid artery and right middle cerebral artery. Computed tomography (CT)-angiography revealed right internal carotid artery (ICA) occlusion from the ICA bifurcation. The patient was diagnosed with atherothrombotic stroke and administered argatroban hydrate, with no further

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Received: December 7, 2020; Accepted: June 4, 2021; Advance Publication by J-STAGE: August 24, 2021
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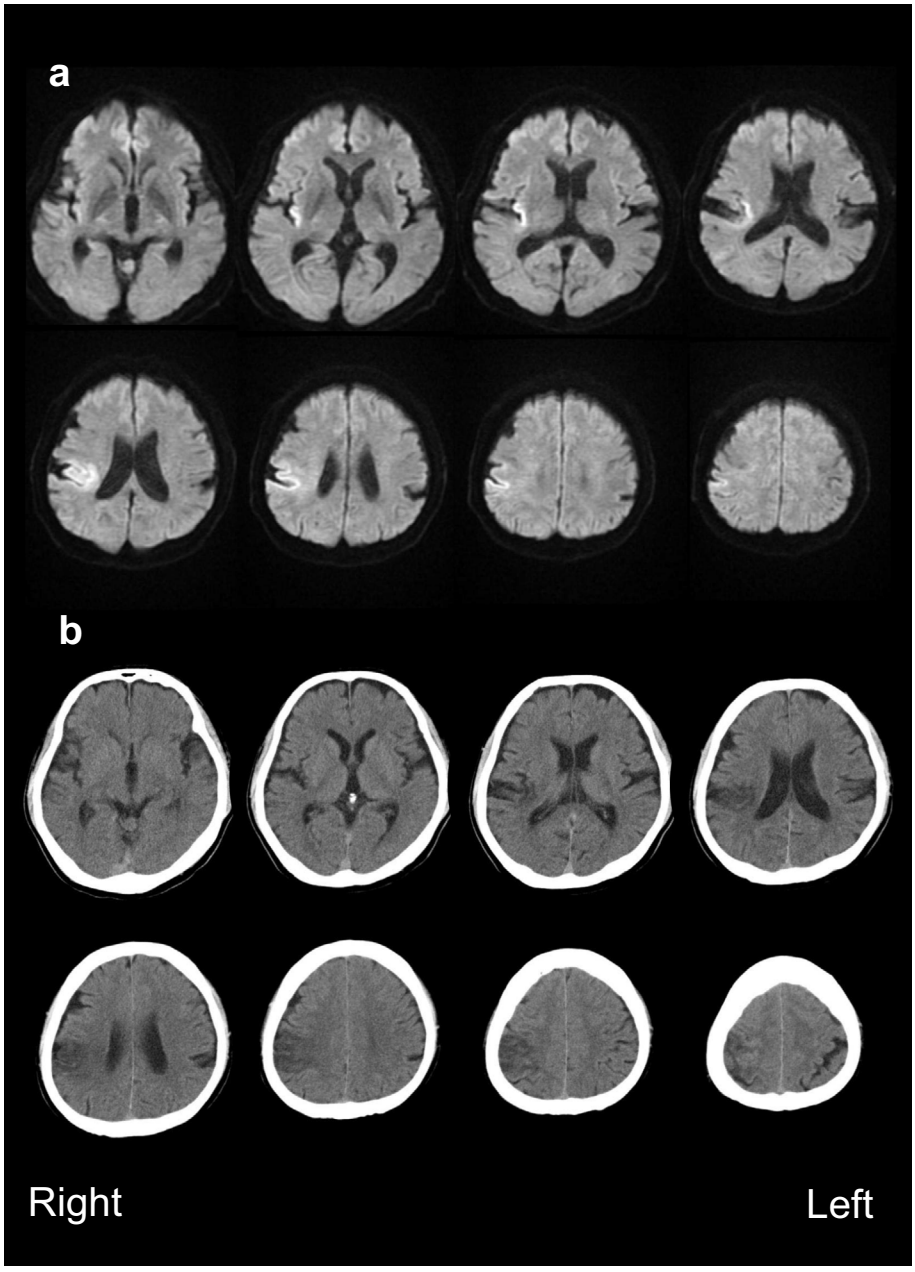

Figure. **(a) Diffusion-weighted magnetic resonance images of the head. High-intensity areas are localized to the upper portion of the right posterior insula, postcentral gyrus, and supramarginal gyrus, as well as the white matter under these structures. (b) Computed tomography images of the head. Low-density areas are localized to the upper portion of the right posterior insula, postcentral gyrus, supramarginal gyrus, and anterior upper portion of the angular gyrus, as well as the white matter under these structures.**

exacerbation of his condition being observed.

Cerebral angiography visualized the middle cerebral artery via the posterior communicating artery. No other vessel showed abnormal findings. Furthermore, articulation returned to normal; however, movement of the left extremities remained encumbered. The patient was transferred to our hospital 23 days after the onset for rehabilitation.

In our hospital, head CT revealed the spread of the infarction to the anterior upper portion of the right angular gyrus; however, there were no other new lesion-related findings (Figure b). Regarding neurological findings, the patient showed mild palsy and clumsiness of the lower and upper left extremities, respectively, with the latter worsening upon eye closing. In addition, he presented with a somatosensory disorder, as described below. There were no other abnormal neurological findings. A neuropsychological examination revealed normal general attention, cognition, and episodic memory. There was a mild reduction in the executive function (Table 1).

The patient provided his written informed consent after receiving a detailed description of the study. This study was approved by the ethics committee of Yamagata Prefectural

Table 1. Results of Neuropsychological Tests.

Test	Performance score
Handedness	
Edinburgh Handedness Inventory (max: 100)	100
General attention	
Digit span	
Forward	6
Backward	4
Spatial span	
Forward	5
General cognition	
Mini-Mental State Examination (max: 30)	30
Episodic memory	
Recall of three words (max: 3)	
Immediate	3
Post-interference	3
He was able to give accurate oral descriptions of the contents of his previous day's training.	
Executive function	
Trail Making Test (s)	
Part A	68
Part B	154
Frontal Assessment Battery (max: 18)	12
Hemispatial neglect	
Catherine Bergego Scale (max: 30)	0

max: maximum, s: seconds

University of Health Sciences and was conducted in accordance with the Declaration of Helsinki.

The patient mentioned the following: "While I was hospitalized in the previous hospital, I felt warmness in my left foot; therefore, I touched the metal bed frame with my left foot to let it cool; however, I did not feel a cold sensation. I considered this strange; therefore, I touched the same frame with my right foot and felt that it was cold. This made me realize that I have reduced sensation in my left foot." We assessed basic somatosensory modalities (6), including pain and temperature sensation, in the bilateral upper and lower extremities (Table 2). For the bilateral upper extremities, we checked for discrimination between two temperatures sensitivity to a temperature increase and decrease and cortical somatosensory modalities (6). The somatosensory tests were performed with shielding to blind the patient from the stimuli and stimulated body parts, with the patient's hands manipulating objects.

Regarding the left side of the body, the patient answered "I cannot feel anything" even after intense pain stimulation in the upper and lower extremities, regardless of whether the stimulated area was proximal or distal. Stimulation mostly elicited no escape response in the upper and lower extremities; however, stimulation at some sites yielded a mild escape response (Table 2). Temperature stimulation revealed that the patient could not perceive warm or cold temperatures. In addition, noxious heat stimulation elicited no escape response, with the patient answering "I cannot feel anything." Noxious cold stimulation elicited a response of "I feel a little discomfort"; however, the stimulus was not perceived as noxious, and there was no escape response. The patient did not show allodynia. He showed marked impairment of tactile sensation and joint position sense; however, there was only a mild reduction in vibration sense.

The patient was unable to discriminate between two different temperatures or perceive increasing or decreasing temperature with his upper left extremity. Regarding cortical somatosensory modalities, there was a marked impairment in two-point discrimination, perception of size and weight, and naming of three-dimensional geometric shapes and everyday items.

For the right side of the body, there was a marked reduction in pain sensation in the upper and lower extremities at all stimulated places, regardless of whether they were proximal or distal (Table 2). At times, the patient remarked "I can feel pressure but no pain" or "I feel a little discomfort" in response to pain stimulation. This surprised the patient since he realized that he lacked sensation in the right leg too. Stimulation mostly elicited no escape response in the upper and lower extremities; however, there was a mild escape response at some sites (Table 2).

The patient could feel warm and cold temperatures in response to temperature stimulation. However, noxious stimulation with high and low temperatures did not elicit any sensation, and there was no escape response. In the lower right extremity, the patient required several seconds of contact with a high-temperature noxious stimulus to feel noxious heat, which also surprised the patient. A low-temperature noxious stimulus did not elicit a noxious cold sensation; however, the patient described it as "very, very cold." An escape response was not elicited by high- or low-temperature noxious stimuli. Allodynia was not observed. There were no other problems with other basic somatosensory modalities.

Regarding the upper right extremity, the patient provided correct answers when discriminating between two different temperatures. The patient had trouble perceiving increasing and decreasing temperature, with this deficit being specifically apparent for increasing temperature. There were no issues observed with cortical somatosensory modalities.

Discussion

Our patient had a lesion involving the upper portion of the right posterior insula and primary somatosensory cortex. He showed a reduced response to noxious stimuli in the left upper and lower extremities contralateral to the lesion, which appeared to be caused by damage to the upper portion of the right posterior insula. Contrastingly, damage to the primary somatosensory cortex may have been involved in the markedly reduced response to most basic somatosensory modalities (excluding noxious stimuli) tested in the left upper and lower extremities and to all cortical somatosensory modalities tested in the upper left extremity.

In addition, the patient showed impaired perception of

Table 2. Somatosensory Test Results.

Tests	Result			
	Left		Right	
	Upper extremity	**Lower extremity**	**Upper extremity**	**Lower extremity**
a. Basic somatosensory modalities				
Pain sensation[†]				
Threshold [load on pin (g); range: 1-20]	>20 at all sites	>20 at all sites	>20 at all sites	>20 at all sites
Escape response to pain stimulus	Mild response at the hypothenar eminence only. No response at other sites.	Mild response at the thumb and middle finger only. No response at other sites.	No response at any site.	Mild response at the proximal and distal site of the dorsal and lower leg, respectively. No response at other sites.
Temperature sensation (stimulation of the palm and distal part of the planta)				
Heat sensation (45°C, 40°C, 35°C, each twice; max: 6)	0	0	6	6
Cold sensation (15°C, 10°C, 5°C, each twice; max: 6)	0	0	6	6
Noxious heat sensation (50°C)	-	-	-	Delayed
Escape response to noxious heat stimulus	-	-	-	-
Noxious cold sensation (-5°C)	-	-	-	-
Escape response to noxious cold stimulus	-	-	-	-
Discriminating between two different temperatures (number of correct answers; max: 6)[‡]	0		6	
Sensitivity to changing temperature[§]				
Increasing temperature (max: 15°C)	>15°C		12°C	
Decreasing temperature (max: 10°C)	>10°C		5°C	
Tactile sensation				
Semmes-Weinstein Monofilament (13) (range: 1.65-6.65)	Thumb >6.65 Little finger >6.65 Thenar eminence >6.65 Lateral side of the dorsal hand >6.65 Distal site on the medial side of the forearm >6.65 Proximal site on the medial side of the forearm 6.65	Big toe 6.65 Little toe 4.31 Ball of the big toe 6.65 Distal side on the dorsal foot 5.07 Medial side of the lower leg 4.31	Thumb 3.61 Little finger 3.61 Thenar eminence 3.61 Lateral side of the dorsal hand 2.83 Distal site on the medial side of the forearm 3.61 Proximal site on the medial side of the forearm 3.61	Big toe 4.31 Little toe 3.61 Ball of the big toe 4.31 Distal site on the dorsal foot 2.83 Medial side of the lower leg 3.61
Vibration sense	Mild impairment		Normal	
Joint position sense (number of correct answers; max: 20)[¶]	0	8	20	19
b. Cortical somatosensory modality				
Two-point discrimination (mm) (stimulation of middle finger tip)	>20.0		2.0	
Size comparison (number of correct answers; max: 6)[a]	0		6	
Weight comparison (number of correct answers; max: 6)[b]	0		6	
Identification of three-dimensional geometric shapes (number of correct answers; max: 6)[c]	0		6	
Identification of everyday items (number of correct answers, max: 12)[d]	0		12	

max: maximum

[†]The thumb, index finger, middle finger, ring finger, little finger, thenar eminence, hypothenar eminence, lateral side of dorsal hand, medial side of dorsal hand, dorsal side of forearm, medial side of forearm, big toe, second toe, third toe, fourth toe, little toe, ball of the big toe, heel, distal site on the dorsal foot, proximal site on the dorsal foot, dorsal side of the lower leg, and medial side of the lower leg were stimulated with a pin. The patient was asked if he felt pain.

[‡]The patient was allowed to freely compare by touch and were asked which was warmer. The temperature combinations administered to the patient were as follows: 45°C/40°C, 40°C/35°C, 45°C/35°C, 15°C/10°C, 10°C/5°C, and 15°C/5°C.

[§]Starting at 20°C, the temperature was raised and lowered at a rate of approximately 0.1°C/s. The patient was asked to inform us as soon as he felt a temperature change. We determined the change in temperature required for the patient to notice a change.

[¶]Joints were moved through approximately 50% and 10% of the joint range of motion on the left and right side, respectively.

[a]From a group of square leather pieces with side lengths of 40 mm, 45 mm, 50 mm, 55 mm, 60 mm, and 65 mm, the patient received two pieces of adjacent sizes (e.g., 40 mm and 45 mm) to touch in succession and was asked which was larger.

[b]From a group of weights of 10 g, 30 g, 50 g, 70 g, 90 g, 110 g, and 130 g that had the same size, the patient received two weights of adjacent weights (e.g., 10 g and 30 g) to hold in succession and asked which was heavier.

[c]From a group of shapes consisting of a sphere, circular cone, cylinder, cube, triangular prism, and hexagonal column, the patient received one shape to handle in a location shielded from the patient's view. Subsequently, all the shapes were shown to the patient and the patient was asked which shape he had handled.

[d]The patient was given a ball-point pen, scissors, spoon, clothes peg, golf ball, or stapler to handle in a location shielded from the view of the patient. He was asked to name the item.

noxious temperature and pain sensation in the right upper and lower extremities ipsilateral to the lesion. These stimuli rarely elicited an escape response. Furthermore, the patient showed trouble perceiving an increasing or decreasing temperature stimulus, especially an increasing temperature stimulus. The ability to sense an increasing or decreasing temperature towards a noxious range is necessary for avoiding danger. Given the aforementioned findings, it seemed that our patient could not obtain the information required to sense impending danger and elicit an instantaneous escape response in the bilateral upper and lower extremities.

Since our patient showed bilateral sensory disorder, we needed to consider peripheral neuropathy as part of the differential diagnosis. The patient did not have a history of diabetes, alcoholism, auto-immune diseases, or vitamin deficiency. As indicated by our pain test results, the sensory disorder did not show a proximal-distal gradient. Furthermore, given that the patient was surprised by the abnormal sensation in the left and right legs after noxious stimulation during hospitalization and tests in the previous and our hospital, respectively, we surmise that the patient presented with an acute onset condition that appeared at around the same time as the cerebral infarction. Moreover, to our knowledge, there have been no reports of peripheral neuropathy where non-noxious temperature sensation, including temperature comparison, was maintained even with loss of noxious temperature and pain sensation. Therefore, the bilateral sensory disorder to noxious stimulation observed in our patient is unlikely to have been peripheral neuropathy.

How unilateral damage of the insula can cause this kind of bilateral impairment remains unclear. The corpus callosum is a cerebral structure through which information regarding noxious stimuli from one side of the body passes before reaching the same side of the insula. However, each cerebral hemisphere can react to highly noxious stimuli in case of damage to the corpus callosum (7). Therefore, our patient's condition cannot be attributed to damage to neural fibers leaving the corpus callosum. The spinal cord contains neurons with a receptive field encompassing both sides of the body that transmit information regarding noxious stimuli. Furthermore, these neurons transmit information to the medial thalamus from the contralateral side of the body via the brainstem reticular formation (8, 9). The observed bilateral impairment in our patient may have been due to the lesion interrupting this information leaving the medial thalamus and intended for the insula.

Several limitations associated with the present study warrant mention. First, in our patient, a unilateral lesion involving the posterior insula reduced the bilateral response to noxious stimuli. However, since the lesion involved other regions, whether or not the lesion in the posterior insula was responsible for this impairment is unclear. Second, the somatosensory test is dependent on the patient's subjectivity and escape response, with missing electrophysiological evidence. Given the similarity between electrophysiological and bedside tests, pinprick-evoked (10) and contact heat-evoked brain potentials (11) can be used for noxious pain and heat sensation, respectively. For warm and cold sensations, amplitude changes observed in 10-Hz electroencephalographic oscillations (12) can be examined. Source dipole modeling performed in these tests can facilitate the investigation of activity of the posterior insula in response to each stimulus type. In the future, we hope that more reports of similar cases of a lesion localized to the posterior insula will be accumulated. If the aforementioned electrophysiological tests are performed on such patients, it may be revealed that the insula opposite the lesion may not be active in its response to noxious stimuli of the limb on the same side and may be active in its response to non-noxious temperature stimuli. This may provide more objective evidence indicating that unilateral damage to the posterior insula can bilaterally impair the sensation of noxious stimuli. Third, the prevalence of bilateral impairment in patients with a unilateral lesion with posterior insula involvement remains unclear. Further large-scale studies should investigate this matter.

The authors state that they have no Conflict of Interest (COI).

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