Original Paper

European Neurology

Eur Neurol 1998;40:151–158

Received: July 28, 1997
Accepted: May 7, 1998

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Contribution of the Supplementary Motor Area and Anterior Cingulate Gyrus to Pathological Grasping Phenomena

Key Words
Supplementary motor area
Anterior cingulate gyrus
Grasp reflex
Instinctive grasp reaction

Abstract
To investigate the relationship between the site of brain damage and characteristics of the pathological grasping phenomena, we examined different varieties of the reaction in a consecutive series of 28 patients with unilateral hemispheric damage due to stroke. Patients with a lesion relatively confined to the supplementary motor area (n = 4) constantly exhibited a grasp reflex, mainly in the hand contralateral to the lesion, but they never showed a groping reaction. By contrast, patients with damage primarily involving the anterior cingulate gyrus (n = 3) developed the groping reaction in the hand contralateral to the lesion, but they had only a very mild grasp reflex in that hand. Patients with damage involving both the supplementary motor area and the anterior cingulate gyrus (n = 12) showed the grasp reflex and groping reaction mainly in the hand contralateral to the lesion. Patients with damage to the medial parietal lobe (n = 2), those with damage to the lateral convexity of the hemisphere (n = 6), and a patient with damage confined to the corpus callosum did not exhibit such grasping phenomena. From these observations, we conclude that the grasp reflex is closely related to a lesion of the supplementary motor area, whereas the groping reaction is bound to a lesion of the anterior cingulate gyrus.

It is well known that some patients with brain damage exhibit pathological grasping phenomena [1–6]. Seyffarth and Denny-Brown [7] identified two distinct types of the phenomenon: a grasp reflex and an instinctive grasp reaction. The grasp reflex is a stereotyped prehensile reaction in response to tactile and proprioceptive stimuli applied to the palm; the instinctive grasp reaction is characterized by more complex and less stereotyped grasping and groping movements of a hand and arm in response to a light touch on a patient's hand or even to a mere visual presentation of an object. They implied that the grasp reflex and the instinctive grasp reaction are based on different neural mechanisms. Recently, De Renzi and Barbieri [8] maintained that the grasp reflex was more common in patients with damage to the anterior cingulate gyrus (ACG). However, they stated no more about responsible lesions for other varieties of the grasping phenomenon.

In the present study, we investigated different varieties of pathological grasping phenomenon in 28 patients with recent unilateral hemispheric damage secondary to

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Table 1. Definition of different varieties of grasping phenomenon

	Stimulus	Response
Grasp reflex	tactile and proprioceptive stimuli applied to the palm	flexion of fingers and adduction of the thumb
Instinctive grasp reaction		
Closing reaction	a light stationary or moving touch on the hollow between thumb and index finger	a sequence of closing movements of the hand that brings the stimulus to the center of the palm
Final grip	a light stationary or moving touch on the hollow between thumb and index finger	a grip of the hand following the closing reaction
Trap reaction	moving tactile stimuli of the examiner's fingers away from the patient's palm	a sudden tightening or flexion of fingers
Magnet reaction	a retreating light touch by the examiner's fingers on the patient's fingertips	pursuing movements of the arm and hand to keep contact with the stimulus
Visual groping	visual presentation of the examiner's hand	pursuing movements of the arm and hand to the stimulus

stroke. To assess the correlation between lesion sites and profiles of the grasping phenomena, we examined all patients by magnetic resonance imaging (MRI).

Materials and Methods

Patients. We prospectively examined 28 patients (18 men, 10 women; ages, 41–81 years) who had recently experienced damage to the unilateral hemisphere. None of the patients had obvious signs of dementia or neurodegenerative diseases before the onset of stroke. Lesions were located on the left in 16 patients and on the right in 12. Twenty-six patients had cerebral infarction and the remaining 2 had intracerebral hemorrhage. Based on the results of a modified Edinburgh inventory [9], 27 patients were right-handed and 1 was ambidextrous. All patients were examined within 6 weeks of the occurrence of stroke. They were all cooperative and were capable of at least some voluntary movements with their affected upper limb.

Examination of Pathological Grasping Phenomena. We elicited pathological grasping phenomena according to the method of Seyffarth and Denny-Brown [7]. Different varieties of the grasping phenomenon are summarized in table 1, where each of the terms is followed by a short definition. We rated the grasp reflex as 'strong' if the patient was unable to inhibit or release the grasp even when explicitly asked to; 'moderate' if the patient found it difficult to inhibit the grasp, but was able to release on verbal command; 'mild' if the grasp was observed only when the patient's attention was diverted from his hand, such as during conversation or calculation; 'minimal' if the grasp was inconstantly observed even when the patient's attention was diverted; and 'absent' if the grasp was not observed at all in several examinations.

We also examined five varieties of the instinctive grasp reaction including closing reaction, final grip, trap reaction, magnet reaction, and visual groping. The stimulus was an examiner's hand. These reactions were recorded as 'present' if the patient often showed fully developed reactions despite being told not to catch the examiner's hand; 'equivocal' if the patient sometimes showed abortive reactions but no responses on other occasions, and 'absent' if the patient did not react at all in several examinations.

Other Neuropsychological Tests. We also sought the following signs: conjugate deviation of the eyes, motor impersistence, anosognosia for the affected limbs, auditory extinction on double simultaneous stimulation, and visual neglect of the left or right hemispace. Conjugate deviation of the eyes was rated as 'present' if the patient's eye movements were incomplete toward the side contralateral to the lesion [10]. Motor impersistence was rated as 'present' if the patient failed to keep the eyes closed for 15 s [10]. Anosognosia was rated as present if patients were unaware or denied their hemiparesis [10]. Auditory extinction was rated as 'present' if the patient consistently ignored the stimulus on one side on simultaneous presentation of snap sounds to both ears [10]. Visual neglect was rated as 'present' if the line cancellation or line bisection test showed neglect of one side [10].

Callosal disconnection sign was also investigated. Callosal disconnection was rated as 'present' if any one of the following signs was present: left unilateral agraphia, left unilateral ideomotor apraxia, and left unilateral tactile anomia [11].

Lesion Analysis. T1- and T2-weighted MRIs were obtained in the axial, coronal and sagittal planes within 2 weeks before or after the examination of grasping phenomena, and were plotted onto standard templates according to the method of Damasio and Damasio [12].

Results

To evaluate the relationship between the location of lesion and the characteristics of the grasping phenomena, we divided patients into 5 groups: patients with a lesion located in the lateral convexity of the hemisphere were

Table 2. Characteristics of grapsing phenomena in all patients

Case No.	Age/Sex	Handedness	Etiology	Lesion side	Days after onset	Contralesional hand						Ipsilesional hand						Other signs
						GR	CR	FG	TR	MR	VG	GR	CR	FG	TR	MR	VG	
Group 1 (lateral group)																		
1	85/M	R	CI	L	16	–	–	–	–	–	–	–	–	–	–	–	–	–
2	75/M	R	CI	L	14	–	–	–	–	–	–	–	–	–	–	–	–	–
3	57/M	R	CI	L	30	–	–	–	–	–	–	–	–	–	–	–	–	–
4	41/M	R	CI	L	25	–	–	–	–	–	–	–	–	–	–	–	–	–
5	70/M	R	CI	R	14	–	–	–	–	–	–	–	–	–	–	–	–	+[a]
6	76/M	R	CI	R	14	–	–	–	–	–	–	–	–	–	–	–	–	–
Group 2 (SMA group)																		
7	71/M	R	CI	L	24	min	–	–	–	–	–	–	–	–	–	–	–	–
8	58/M	R	CI	L	28	min	–	–	–	–	–	–	–	–	–	–	–	–
9	62/M	R	CI	R	6	mi	–	–	+	–	–	–	–	–	–	–	–	–
10	81/F	R	CI	R	26	str	+	+	+	–	–	mod	+	+	+	–	–	–
Group 3 (ACG group)																		
11	57/M	R	CI	L	29	min	+	+	+	+	+	–	–	–	–	–	–	–
12	72/F	R	CI	L	14	min	+	+	+	+	+	–	–	–	–	–	–	–
13	52/F	R	CI	L	30	min	±	±	±	±	±	–	–	–	–	–	–	–
Group 4 (SMA + ACG group)																		
14	75/M	R	CH	L	38	mod	+	+	+	±	–	–	–	–	–	–	–	–
15	41/F	R	CI	L	24	mod	+	+	+	+	+	–	–	–	–	–	–	+[b]
16	80/F	R	CI	L	30	mod	+	+	+	+	+	–	+	+	+	–	–	–
17	75/F	R	CI	L	21	mod	+	+	+	+	+	mi	+	±	+	±	±	–
18	51/F	R	CI	L	40	str	+	+	+	+	+	–	–	–	–	–	–	–
19	46/F	R	CI	L	17	mod	+	+	+	+	+	–	–	–	–	–	–	–
20	45/M	R	CI	R	13	str	+	+	+	+	+	–	–	–	–	–	–	–
21	46/F	R	CI	R	42	mi	+	+	+	+	+	–	±	–	+	–	–	–
22	58/F	R	CI	R	33	str	+	+	+	+	+	mi	+	+	+	+	+	–
23	51/M	R	CI	R	42	mod	+	+	+	+	+	–	–	–	–	–	–	–
24	46/M	Ambi	CI	R	35	str	+	+	+	+	+	mi	+	–	+	–	–	+[b]
25	50/M	R	CI	R	18	mod	+	+	+	±	±	–	–	–	–	–	–	–
Group 5 (Posterior cingulate or corpus callosum group)																		
26	69/M	R	CH	L	13	–	–	–	–	–	–	–	–	–	–	–	–	–
27	44/M	R	CI	R	42	–	–	–	–	–	–	–	–	–	–	–	–	–
28	73/F	R	CI	R	33	–	–	–	–	–	–	–	–	–	–	–	–	–

M = Male; F = female; R = right; L = left; Ambi = ambidextrous; CI = cerebral infarction; CH = cerebral hemorrhage; GR = grasp reflex; CR = closing reaction; FG = final grip; TR = trap reaction; MR = magnet reaction; VG = visual groping; str = strong; mod = moderate; mi = mild; min = minimal; + = present; ± = equivocal; – = absent.

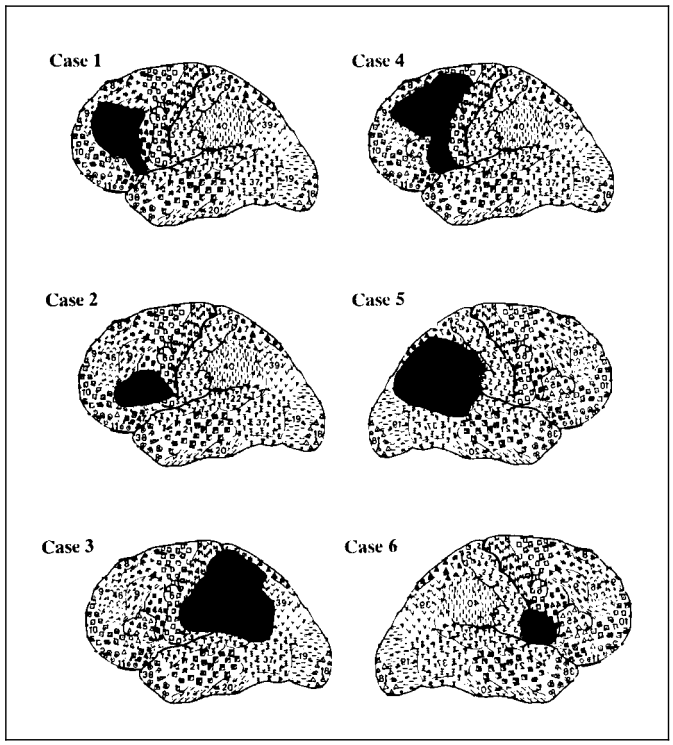
[a] Left-sided auditory extinction and visual neglect.

[b] Left unilateral ideomotor apraxia.

assigned to group 1; patients with a lesion relatively confined to the SMA, to group 2; those with a lesion primarily involving the ACG, to group 3; those with a lesion involving both the SMA and ACG, to group 4, and those with a lesion involving the posterior cingulate gyrus or with a lesion confined to the corpus callosum, to group 5.

The characteristics of grasping phenomena and associated neuropsychological signs of the patients are summarized in table 2.

In group 1, the lesion was located on the left in 4 patients (cases 1–4) and on the right in 2 (cases 5, 6) (fig. 1). Two patients (cases 1, 4) had damage to the lateral



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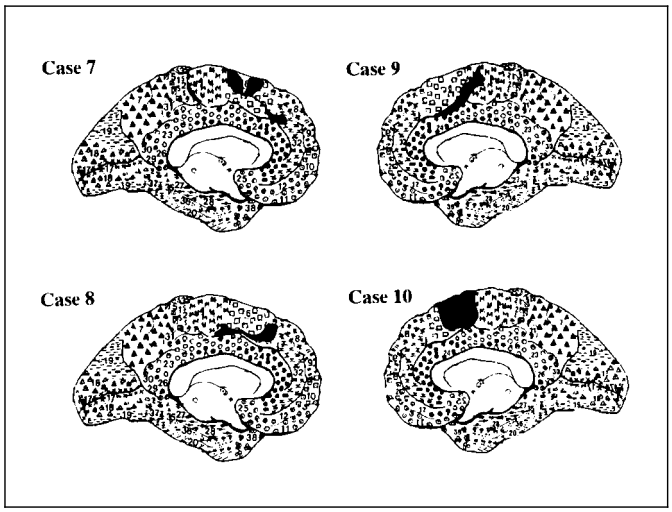

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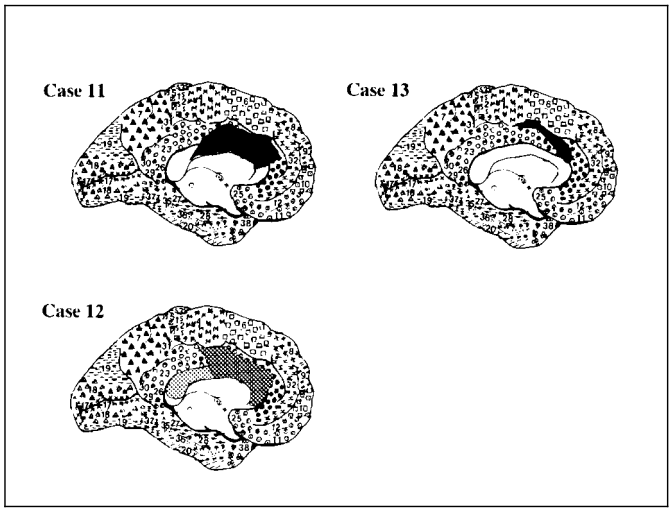

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Fig. 1. Schematic lateral hemispheric lesions of group 1 patients. The black areas represent very high intensity T2-weighted MRI signals.

Fig. 2. Schematic medial hemispheric lesions of group 2 patients. The black areas represent very high intensity T2-weighted MRI signals.

Fig. 3. Schematic medial hemispheric lesions of group 3 patients. The black, crosshatched, and shaded areas correspond to regions of very high, moderately high, and mildly high intensity T2-weighted MRI signals.

premotor and lateral prefrontal area; another 2 patients (cases 2, 6) had a lesion involving the frontal opercular area; and the remaining 2 patients (cases 3, 5) had damage to the lateral parietal area. Case 5 exhibited the left hemispatial neglect and left-sided auditory extinction. No patients in this group demonstrated pathological grasping phenomena.

In group 2, the lesion was located on the left in 2 patients (cases 7, 8) and on the right in 2 (cases 9, 10; fig. 2). Damage to the SMA was partial in 3 patients (cases 7–9) and was more extensive in 1 (case 10). Although the lesions of 3 patients (cases 7–9) extended near the dorsal bank of the cingulate sulcus, none of them had severe damage to the sulcus. The patients with partial damage to the SMA showed a mild or minimal grasp reflex in the contralesional hand. Case 9 also showed a trap reaction in the contralesional hand. The remaining 1 patient (case 4) with extensive lesion in the right SMA demonstrated a strong grasp reflex and the closing reaction, final grip, trap reaction in the contralateral left hand. The patient also showed a moderate grasp reflex, closing reaction, final grip and trap reaction in the ipsilateral right hand. Magnet reaction and visual groping were never elicited in this group of patients.

In group 3, all 3 patients (cases 11, 12, 13) had a left-sided lesion. Damage to the ACG was partial in 1 patient (case 13), and was extensive in 2 (cases 11, 12). All lesions extended to the cingulate sulcus. In case 11, the lesion involved a large part of the ventral bank of the sulcus. Case 12 had comparable damage to that area, although it

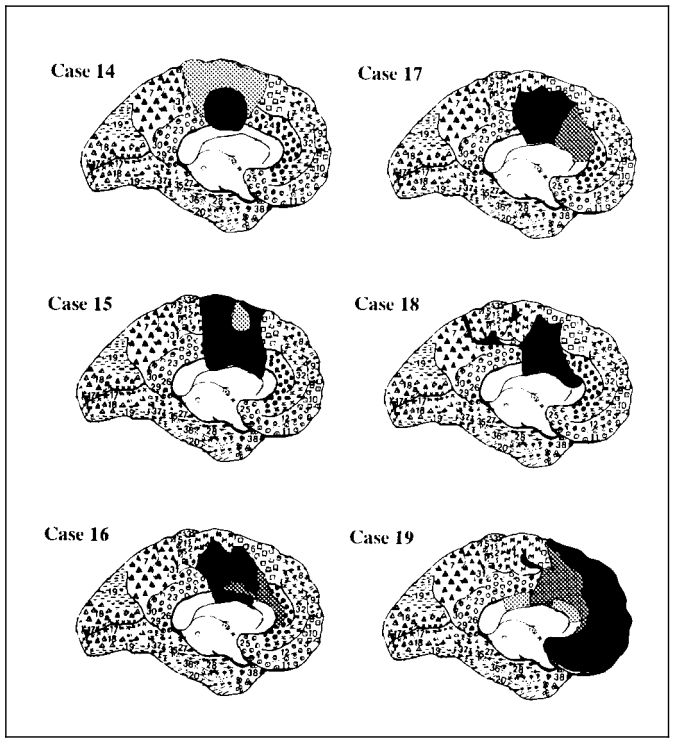

Fig. 4. Schematic left medial hemispheric lesions of group 4 patients. The black, cross-hatched, and shaded areas correspond to regions of very high, moderately high, and mildly high intensity T2-weighted MRI signals. An exception is case 14, where the black area represents low-intensity T2-weighted MRI signals due to hemorrhage, and the surrounding shaded area represents high-intensity T2-weighted MRI signals due to edema.

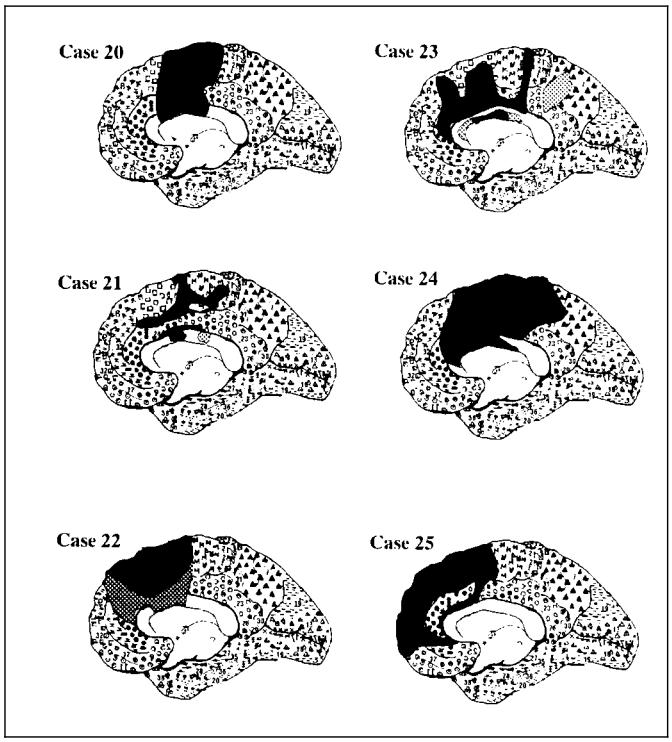

Fig. 5. Schematic right medial hemispheric lesions of group 4 patients. The black, cross-hatched, and shaded areas correspond to regions of very high, moderately high, and mildly high-intensity T2-weighted MRI signals.

mainly involved the subcortex. Case 13 had a lesion that involved both the ventral and dorsal bank of the sulcus. Cases 11 and 12 had damage to the genu and body of the corpus callosum as well (fig. 3). All patients demonstrated a minimal grasp reflex and all varieties of the instinctive grasp reaction, including the magnet reaction and visual groping, in the contralateral right hand.

In group 4, the lesion was located on the left in 6 patients (cases 14–19) and on the right in 6 patients (cases 20–25). All lesions extended into the cingulate sulcus. All patients except 2 (cases 14, 25) had damage to the corpus callosum as well (fig. 4, 5). All but 1 patient (case 21) exhibited a moderate or strong grasp reflex in the contralesional hand. Case 21 had only partial damage to both the SMA and ACG, and showed a mild grasp reflex in the contralesional hand. All varieties of the instinctive grasp reaction were constantly observed in the contralesional hand in this group of patients except for cases 14 and 25. In case 14, the magnet reaction was equivocal and visual groping was absent. In case 25, both responses were equivocal. Ipsilateral grasp reflex and/or instinctive grasp reaction, although they were less prominent than the contralateral ones, were observed in 5 patients (cases 16, 17, 21, 22, 24).

In group 5, the lesion was located on the left in 1 patient (case 26) and on the right in 2 patients (cases 27, 28). Two patients (cases 26, 27) had a lesion involving the posterior cingulate gyrus and medial part of the parietal lobe. The lesion of case 27 extended to the body of the corpus callosum. Case 28 had a lesion confined to the body of the corpus callosum (fig. 6). No patients in this group showed pathological grasping.

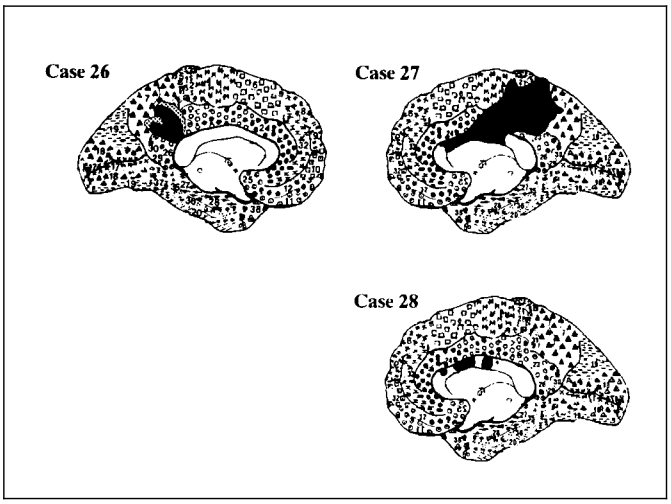

Fig. 6. Schematic lesions of group 5 patients. Black areas represent high-intensity T2-weighted MRI signals, except for case 26, where the black area represents low T2-weighted MRI signals.

Discussion

Our major findings in this study are summarized as follows: (1) all 4 patients with lesions relatively confined to the SMA exhibited the grasp reflex, and in addition, some varieties of the instinctive grasp reaction, mainly in the hand contralateral to the lesion, but they never exhibited the magnet reaction and visual groping; (2) all 3 patients with a lesion primarily involving the ACG showed all varieties of the instinctive grasp reaction, including the magnet reaction and visual groping, in the hand contralateral to the lesion, but they exhibited a minimal grasp reflex in that hand; (3) almost all patients with extensive lesions involving the SMA and ACG showed a moderate or strong grasp reflex and all varieties of the instinctive grasp reaction, mainly in the hand contralateral to the lesion; (4) some patients showed grasping phenomena also in the hand ipsilateral to the lesion, although they were less prominent than those in the hand contralateral to the lesion; (5) no pathological grasping phenomena were observed in patients with a lesion confined to the lateral convexity of the hemisphere, with a lesion involving the posterior cingulate gyrus and medial parietal lobe, or with a lesion on the body of the corpus callosum.

From these observations, we suggest that the grasp reflex is closely related to the SMA lesion, while the magnet reaction and visual groping are tightly linked to the ACG lesion. Other different varieties of the instinctive grasp reaction, including the closing reaction, final grip and trap reaction, were not distinctive from the grasp reflex in terms of their responsible lesion. The latter conclusion is in agreement with the assertion of De Renzi and Barbieri [8] that, at least in a clinical situation, a too fine-grained categorization of the grasping phenomena is unrewarding and they may be categorized into the grasp reflex and groping responses (magnet reaction and visual groping).

There may be a claim that some of the lesions of group 2 (SMA group) patients also involved the regions of the cingulate sulcus, which correspond to the cingulate motor areas (CMAs) identified in monkeys within the dorsal and ventral banks of the cingulate sulcus [13–17]. However, the damage to the cingulate sulcus in group 2 patients appeared to be less extensive than that in group 3 (ACG group) patients. Therefore, we believed that our group categorization is fairly reasonable.

We also found that some patients exhibited ipsilateral grasp reactions. Regarding to this, an article by Mori and Yamadori [10] is interesting. They reported that some patients with a large hemispheric lesion or a subcortical lesion showed an instinctive grasp reaction in a hand ipsilateral to the lesion. They found that the ipsilateral instinctive grasp reaction was more frequently observed in patients with right-hemispheric damage, and that the reaction was highly correlated with various right-hemispheric behavioral syndromes such as conjugate deviation of the eyes, motor impersistence, anosognosia for the affected limbs, auditory extinction on double simultaneous stimulation, and visual neglect of the left hemispace. However, none of our patients with grasping exhibited such right behavioral syndromes. Moreover, the grasping phenomena in our patients were not voluntary movements caused by comprehension deficits; when the examiner asked the patients why they grasped or seized, several patients said, 'My hand grasps or moves unintentionally,' 'My hand moves by itself just as if you had a magnet or something like that,' or 'It's strange that may hand pursues your hand.' Thus, our subjects appeared to be different from those of Mori and Yamadori in terms of location and size of lesions and associated neuropsychological abnormalities. For the present, it would be wise to discuss the basis of the grasping phenomena separating patients like ours from those with many other neuropsychological disturbances, especially with right behavioral syndromes.

Anatomical Basis of the Pathological Grasping Phenomena

The SMA and the primary motor cortex receive direct projections from the primary somatosensory cortex [18]. The SMA has reciprocal connections with the primary motor cortex, the anterior cingulate cortex and the lateral premotor cortex [18, 19]. These cortico-cortical connections suggest that the SMA is able to transmit afferent input to the primary motor area from peripheral somatosensory receptors. Single-unit recordings in monkeys [19] have shown that some neurons in the SMA respond to tactile stimuli and to passive movements of the limbs. The most effective somatosensory stimulus is proprioception such as joint movements [20]. Wiesendanger et al. [21] have also suggested that some cells in the SMA may act as a gate for somatosensory input to the primary motor cortex. The implication from these studies is that a group of neurons in the SMA could have inhibitory effects on the primary motor cortex based on information from the somatosensory cortex. If so, damage to the SMA would cause the grasp reflex because its inhibitory effect on the input of somatosensory stimuli to the primary motor cortex would be removed. It should be noted also that, in this study, grasping phenomena in a hand ipsilateral to the lesion were observed only in patients with a lesion involving the SMA. It is well known in monkeys that the two SMAs have profound reciprocal connections [22]. Thus, it is possible that an extensive damage to unilateral SMA would cause a dysfunction of another, resulting in bilateral grasping phenomena.

As for the ACG, recent studies in monekys have revealed that there are multiple nonprimary motor areas (CMAs) in the depths of the cingulate sulcus [13–17]. The CMAs project directly to the lateral premotor area as well as to the SMA and to the spinal cord [18, 23, 24]. There are lines of evidence in monkeys and humans that this lateral motor area plays a pivotal role in tactile exploration and reaching and grasping movements in response to rather complex somatosensory and visual stimuli [25, 26]. In contrast to the lateral premotor area, recent autoradiographic studies in monekys showed that the dorso-caudal part of the CMA was activated when remembered (self-paced) sequences of reaching movements were executed [27], but was not activated with simple reaching movements guided by visual cues [28]. These studies imply that the CMA is activated differently from the lateral motor area in terms of controlling reaching movements. It could be that the CMAs have a function in modulating activities of the lateral motor area in response to external stimuli. If so, damage to the CMAs would cause automatic responses of the lateral motor area to external stimuli, resulting as the magnet reaction and visual groping.

The lesions of patients with groping responses in this study were extensive to the surface of the ACG as well. Although the surface of the ACG is not known to contain movement-related neurons, it could possibly have an influence upon motor behaviors. Indeed, Petit et al. [29] showed in a positron emission tomography study that both cortices in the depths of the cingulate sulcus and of the midcingulate gyral surface were involved in response selections associated with saccadic eye movements in humans. It may be more likely that combined damage to the CMAs and to the surface of the ACG is crucial to develop groping responses.

Acknowledgments

We are grateful to Drs. Taminori Obayashi (Department of Clinical Pathology, Jichi Medical School) and Colum D. MacKinnon (Human Movement and Balance Unit, The Institute of Neurology, Queen Square) who reviewed this manuscript critically. We are also thankful to Drs. Toshiyuki Maki and Seiji Hasegawa (Department of Neurology, Kameda Medical Center), Dr. Jin Kaneko (Department of Neurology, Ohta General Hospital), Dr. Tetshushi Atsumi (Department of Neurology, Seirei Hamamatsu Hospital), Dr. Akira Imai (Department of Neurology, Utsunomiya Saiseikai Hospital), Dr. Toshiya Fukui (Department of Neurology, Showa University Hospital), Dr. Ryo Sakuma (Department of Neurology, Yamagata Saiseikan Hospital), Dr. Yasumasa Tabuchi (Neurology Service, Hyogo Brain and Heart Center at Himeji), Dr. Kamo Tsutomu (2nd Department of Internal Medicine, St. Marianna University School of Medicine), and Ms Mutsuko Sato (Department of Neuropsychology, Southern Research Institute for Neuroscience) for referring patients to us.

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