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Short communication

Dementia mimicking a sudden cognitive and behavioral change induced by left globus pallidus infarction: Review of two cases

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Abstract

Recently there has been increasing interest in the non-motor functions of the globus pallidus, and especially its role in cognitive processing. We experienced two patients with acute cognitive and behavior changes after globus pallidus infarctions. Examination of both revealed inattention, decreased verbal fluency, emotional blunting, and amnesia. There were no other sensory or motor symptoms. Brain magnetic resonance imaging (MRI) showed focal acute cerebral infarction in the left globus pallidus. Neuropsychological assessment revealed decreased frontal executive function, with verbal memory disturbance. These cases suggest that strategic infarction dementia can result from a single globus pallidus lesion. © 2008 Published by Elsevier B.V.

Keywords: Globus pallidus; Basal ganglia; Cerebral infarction; Cognition; Behavior

1. Introduction

The basal ganglia participate in cognitive activities as well as motor functions. Many reports have suggested that the basal ganglia, particularly the striatum, play an integrative role in cognitive information processing [1-3]. Recently there has also been increasing interest in the nonmotor functions of the globus pallidus, especially regarding their role in cognitive processing. A few clinical studies have reported that bilateral globus pallidus lesions cause mood or cognitive disorders primarily [4,5]. We report two cases that presented with behavioral and cognitive dysfunction without motor symptoms after focal left globus pallidus infarctions.

2. Case reports

2.1. Case 1

A 71-year-old right-handed man was admitted for abnormal behavior that began about 3 days before admission. His wife

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said that he had previously had a great appetite, and had been unable to control his desire for food. However, just before admission, he stopped eating. In addition, his character became much more subservient. Examination of the patient revealed mild disorientation, inattention, memory disturbance, decreased verbal fluency, and emotional blunting. There were no other sensory or motor symptoms.

He had had diabetes mellitus for 20 years, and hypertension for 5 years but no history of psychiatric illness or alcohol or drug abuse. The blood work-up was normal. MR imaging was obtained by using a 1.5 T MR imaging scanner. Brain magnetic resonance imaging(MRI) showed a high intensity signal in the left basal ganglia, mainly in the left globus pallidus (Fig. 1). The first neuropsychological assessment performed at 7 days after admission, showed gross reduction in most areas of cognitive function except for attention (Table 1). After 3 months, the patient had shown significant improvement on language and visuospatial function although frontal executive dysfunction (decreased verbal fluency, disinhibition) and verbal memory disturbance remained affected. The recall trial on visual memory test also showed improvement however sustained a poor score on recognition trial (Table 1).

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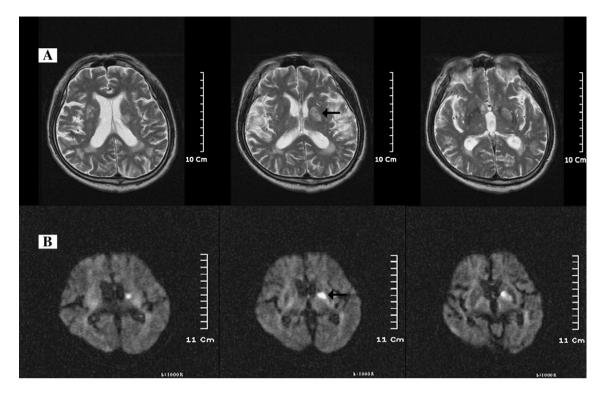


Fig. 1. Axial T2-weighted (A) and diffusion-weighted (B) MRI of the first patient showing a high signal intensity lesion (arrow) in the left globus pallidus and multiple old ischemic lesion in bilateral basal ganglia with diffuse cortical atrophy.

2.2. Case 2

A-48-year-old man presented to our memory disorder clinic because of change in personality. He had difficulty concentrating, with memory impairment, poor self-esteem, and social isolation. The symptoms appeared abruptly 5 days before his initial visit. His wife said that he had previously been a healthy, active, and positive person, but had become depressed and demoralized. Moreover, while he had previously smoked one and a half pack of cigarettes a day for 20 years, he no longer experienced pleasure from smoking, and quit as a consequence. The neurological examination revealed emotional blunting, auto-activation deficit, decreased verbal fluency and memory disturbance with no other motor or sensory symptoms. T2-weighted and diffusion-weighted MRI revealed a focal high signal intensity lesion in the left globus pallidus (Fig. 2). A neuropsychological assessment performed 2 weeks after admission revealed frontal/executive dysfunction (decreased verbal fluency, disinhibition), with verbal memory disturbance, and deficit of language and related functions (comprehension, confrontational naming, ideomotor apraxia). Visuospatial dysfunction was also noted (Table 1). On visual memory test, recall trial was normal however recognition score was poor.

3. Discussion

This report describes acute left globus pallidus infarctions that manifest as sudden changes in cognition and behavior.

The two patients in this report had symptoms in common that were similar to those of frontal lobe syndrome, including inattention, decreased verbal fluency, emotional blunting, reduced spontaneous activity, and memory disturbance, while they did not have any motor or sensory symptoms. There have been a few reports which mention that bilateral lesions of pallidal or lentiform nucleus can cause cognitive and behavioral disturbances along with movement disorders [6]. However, reports focusing on unilateral damage to the globus pallidus are relatively rare, especially those associated with behavioral consequences.

The current understandings of the corticostriatal projections and their maintenance through the basal ganglia circuitry enables us to explain the cognitive deficits and behavior changes seen in our patients. The basal ganglia constitute a major information integrative processing system from the cerebral cortex, and redistribute these integrated signals towards motor, prefrontal, and limbic cortical areas via thalamic nuclei [7,8]. Topographically, the corticostriatal projections are organized so that different cortical areas project to the respective striatal areas. This topographic arrangement imposes a functional subdivision of the striatum into dorsolateral 'somatosensory' (movement), intermediate 'associative' (cognitive functions), and ventromedial 'limbic' (emotional-motivational behaviors) fields that entertain different parts of the frontal lobe, *i.e.*, the premotor, dorsolateral prefrontal, and orbitomedial prefrontal cortices [9,10]. This topographic arrangement of the striatal afferents projects to the globus pallidus, according to the three pallidal

| Neuropsychological | evaluation in 2 | patients with | left globus | pallidus infarction |
|--------------------|-----------------|---------------|-------------|---------------------|
| | | | | |

| | | The 1st patient | The 2nd patient | |
|---------------------------------------|-------------------------------|------------------------------------|---------------------------------------|-------------------------------|
| | | First assessment (7 days after) | Second assessment (3 months after) | Assessment (2 weeks after) |
| | | | | |
| Attention | | | | |
| Digit spam (Forward/backward) | | 4(22.4%ile)/(<1%ile) | 4(22.4%ile)/0(<1%ile) | 6(50%ile)/3(30.5%ile) |
| Language and | related functions | | | |
| Comprehensive | | Normal | Normal | Abnormal |
| Repetition | | Abnormal | Normal | Normal |
| Naming test | | 7/15 (5.2%ile) | 32/60(13.4%ile) | 32/60(1.1%ile) |
| Praxis | | Abnormal | Normal | Abnormal |
| Right-left orientation | | Abnormal | Normal | Normal |
| Calculation | | Abnormal | Normal | Normal |
| Visuospatial fu | nction | | | |
| Copying Rey-Osterrieth complex figure | | 9.5/36(<11%ile) | 26.5/36(13.4%ile) | 30.5/36(<1%ile) |
| Memory | | | | |
| Verbal learning | g test | | | |
| Immediate recall | | 5/36(<1%ile) | 7/36(1.2%ile) | 12/36(2.0%ile) |
| Delayed recall | | 0/12(<1%ile) | 0/12(<1%ile) | 0/12(<1%ile) |
| Recognition score | | 11/24(<1%ile) | 15/24(<1%ile) | 16/24(<1%ile) |
| Rey-Osterrieth | n complex figure | | | |
| Immediate recall | | 0/36(<1%ile) | 10.5/36(34.8%ile) | 8.5/36(18.7%ile) |
| Delayed recall | | 0/36(<1%ile) | 11.7/36(43.6%ile) | 11/36(18.7%ile) |
| Recognition score | | 16/24(3.8%ile) | 15/24(<1%ile) | 15/24(2.2%ile) |
| Frontal executi | ive function | | | |
| COWAT | Semantic (Animal/Supermarket) | 2(<1%ile)/2(<1%ile) | 6(1.2%ile)/0(<1%ile) | 8(<1%ile)/8(<1%ile) |
| | Phonemic | NA | NA | 6(1.1%ile) |
| Stroop test (word/color) | | NA | 66(<16%ile)/18(<1%ile) | 110(<16%ile)/3(<1%ile) |
| MMSE | | 19 | 22 | 22 |
| Geriatric depression scale | | 18 | 16 | 15 |
| Clinical dementia rating | | 2 | 0.5 | 1 |

Abbreviation: MMSE, Mini Mental State Examination; COWAT, Controlled oral Word Association Test.

territories, *i.e.*, motor, associative, and limbic fields [11]. In our cases, the disruption of the fronto-subcortical circuits at the level of the pallidum resulted in symptoms similar to frontal lobe syndrome.

Although the first patient showed more significant decline in overall cognitive function possibly due to age and old ischemic lesions, the neuropsychological assessment of both patients revealed some common traits of decline in frontal/ executive function (decreased verbal fluency, disinhibition) and verbal memory quite significantly.

We thought that the first assessment results of the patients may have presented worse as they were assessed during an acute situation. However, when repeated after 3months on our first case patient, the deficits remained in the above two areas, and the rest improved.

Therefore we concluded that these dysfunctions are truly as a result of the global pallidus infarct. A few researches about neuropsychological change following pallidotomy showed similar results to those seen in our patients that people with left-sided lesion showed significant decline in category verbal fluency and verbal learning test [12,13]. On analyzing the results of verbal memory test, we concluded that the patients had memory dysfunction at encoding and at retrieval processes because of significant decline in free recall as well as cued recall. During verbal memory encoding, prefrontal activation was strongly associated with intentional verbal encoding, whereas left medial temporal activation was crucial for successful formation of declarative memories [14]. Therefore memory disturbance of our patients may be attributed by dysfunction of prefrontal cortex due to disruption of fronto-subcortical circuits.

Furthermore, the reports about globus pallidus activation during verbal working memory in functional MRI could also support our hypothesis [15]. During visual memory test, the patients showed significant decline only in recognition trial due to excessive false positive errors. These results also reflect frontal/executive dysfunction.

This prominent decline in verbal memory more than in visuospatial memory can be explained by lesion laterality, that left pallidal lesion group shows more significant decline

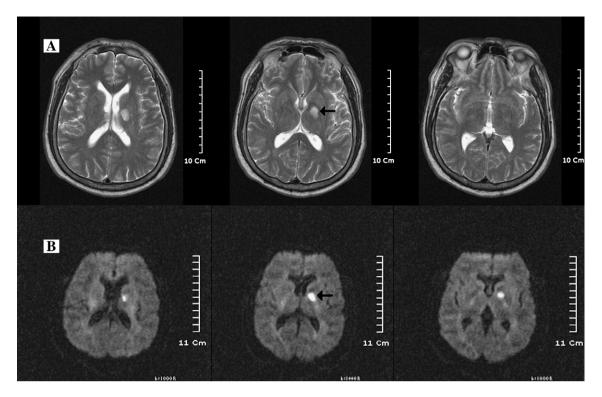


Fig. 2. Axial T2-weighted (A) and diffusion-weighted (B) MRI of the second patient showing a focal high signal intensity lesion (arrow) in the left globus pallidus. There are no other abnormalities of the brain.

in verbal fluency and verbal learning than right lesion group [13,16].

The fact that our patients showed only cognitive and behavioral deficits, without any movement disorders, concurs with the theory that each circuit involves its own area of the globus pallidus, as mentioned above. Grabli et al. demonstrated this functional diversity and territorial specificity of the globus pallidus by microinjecting bicuculline into the external globus pallidus in monkeys; abnormal movements were observed when the posterior part of the external globus pallidus was lesioned, whereas anterior injuries produced behavioral changes [11]. They concluded that the anterior part of the globus pallidus was related to limbic and associative sectors. In our patients, diffusion-weighted MRI showed focal high signals located in the ventral part of the globus pallidus (Figs. 1 and 2). These findings explain the presence of behavioral symptoms in our patients, without motor symptoms.

There have been a few reports about behavior changes associated with selective globus pallidus lesions in humans. Personality changes, including abulia, indifference, and indecisiveness, have been reported in a patient after climbing a high mountain; the T2-weighted MRI revealed high signal lesions in the globus pallidus bilaterally [4].

Anhedonia, difficulties concentrating and remembering, and social isolation after hypoxic episodes resulting from selective bilateral globus pallidus lesions, have recently been reported [5]. However, in these reports, the lesions were bilateral and diffuse. In addition, those patients had movement symptoms as well as behavioral changes. Since, those cases resulted from hypoxic events, one cannot rule out the possibility that diffuse hypoxic brain damage caused the cognitive and behavioral deficits. By contrast, our patients each had a focal globus pallidus lesion resulting from an acute cerebral infarction.

Another interesting feature in our patients was the loss of desire for food or for cigarettes after a globus pallidus infarction, although the patients had not been able to control these desires previously. The brain reward circuit may explain these findings, because the ventral pallidum is part of brain reward circuit, which includes the ventral tegmental area, which projects dopaminergic fibers to the nucleus accumbens and globus pallidus [5]. Limbic cortical areas are associated with the hypothalamus and ventral pallidum, via the nucleus accumbens. In addition, the nucleus accumbens projects fibers to the ventral tegmental area through the ventral pallidum [17]. This circuit generates a reward hedonic impact and incentive motivation for food, addictive drugs, and other rewards [18]. Therefore, we suggest that damage to the ventral pallidum resulted in the loss of the cravings for food and smoking in our patients.

It is well understood that the lesions of globus pallidus commonly causes movement disorders, such as dystonia or parkinsonism and sometimes behavioural disturbances, particularly when the bilateral pallidal areas are involved. However, our case reports showed that unilateral lesions of globus pallidus could induce isolated behavioral changes and cognitive dysfunction, similar to strategic infarct dementia. Therefore, we suggest that the globus pallidus, especially the ventral portion of the dominant hemisphere, is one possible site causing strategic infarct dementia.

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