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Case Report / Olgu Sunumu

Frontal Lobe Syndrome Due to Striatocapsular Infarction

Striatokapsüler Enfarkta Bağlı Frontal Lob Sendromu

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Abstract

The frontal lobes are important in human cognition and are involved in aspects such as executive functioning and social cognition. These domains are broadly subsumed under the rubric of frontal functions. Human cognition is subserved by large-scale neural networks with subcortical and cortical components. Therefore, frontal lobe syndrome should be understood as the clinical consequence of damaged parallel frontostriatal circuits in the frontal lobes. While these manifestations may evolve progressively during neurodegenerative processes (e.g., frontotemporal dementia), they may appear acutely or full-blown after a strategically located infarction within a specific neural network, whether a cortical or subcortical hub. Here, the author reports a case of a 70-year-old woman with acute onset of apathy, restlessness, and hyperorality. A mental status examination showed perseverations, decreased resistance to interference, and a left-sided hemineglect. Magnetic resonance imaging revealed a right-sided striatocapsular infarction. One year later, a ^{18}F-fluorodeoxyglucose-positron emission tomography scan showed large ipsilateral frontal and contralateral cerebellar hypometabolism compatible with diaschisis. An acute onset of a complex clinical presentation involving most of the functions of a single hemisphere may be seen after a strategically located single cerebral infarction. Basal ganglia structures, such as the right-sided caudate and anterior putamen, may host the hubs that comprise large-scale networks for executive functions, social cognition, and directed attention. Behavioral-cognitive syndromes should be evaluated as a manifestation of network damage.

Keywords: Frontal lobe syndrome, basal ganglia, infarction, caudate nucleus, hyperorality

Öz

Frontal loblar yürütücü işlevler ve sosyal kognisyon gibi alanlar da dahil olmak üzere insan kognisyonunda önemli bir role sahiptir. Bu alanlar genel olarak frontal işlevler başlığı altında toplanır. İnsan kognisyonu, kortikal bileşenlerin yanı sıra subkortikal bileşenlere de sahip olan geniş boyutlu nöral ağlar tarafından yürütülmektedir. Bu nedenle frontal lob sendromu olarak adlandırılan frontal işlev bozukluğu, frontal loblarda yerleşik paralel frontostriatal devrelerin hasar görmesinden kaynaklanabilir. Bu tezahürler nörodejeneratif süreçler (örneğin; frontotemporal demans) sırasında progresif olarak gelişirken, belirli bir sinir ağı içinde kortikal veya subkortikal bir bileşende stratejik olarak konumlandırılmış bir enfarktüsün ardından akut olarak da ortaya çıkabilirler. Bu makalede akut başlangıçlı apati, huzursuzluk ve hiperoralite nedeniyle değerlendirilen 70 yaşında bir kadın hasta sunulmaktadır. Mental durum muayenesinde perseverasyonlar, çeldiricilere azalmış direnç ve sol yarı mekan ihmali saptanan hastanın manyetik rezonans görüntülemesinde sağ striato-kapsüler enfarktüsü mevcuttu. Bir yıl sonra yapılan ^{18}F-florodeoksiglukoz pozitron emisyon tomografi görüntülemede, diaşizis ile uyumlu büyük ipsilateral frontal ve kontralateral serebellar hipometabolizma gözlendi. Tek bir hemisferin fonksiyonlarının çoğunda bozulmayı içeren akut başlangıçlı bir hasar stratejik yerleşimli bir serebral enfarktüs sonrasında görülebilir. Sağ tarafta kaudat ve anterior putamen gibi bazal ganglia yapıları, yürütücü işlevler, sosyal kognisyon ve mekansal dikkat için büyük ölçekli ağların merkezlerini barındırabilir. Davranışsal-kognitif sendromlar, geniş boyutlu kognitif ağ hasarının bir belirtisi olarak değerlendirilmelidir.

Anahtar Kelimeler: Frontal sendrom, bazal ganglia, enfarktüs, kaudat çekirdek, hiperoralite

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Introduction

The unique personality structure of a human individual, which is subjective, is determined by the frontal lobes. Personality change is a well-known consequence of frontal lobe damage, as taught by the inaugural case of Phineas Gage. Behavioral changes, such as apathy and impulsivity, and the cognitive changes in executive functions observed in Gage (and the following reported cases) were collectively coined "frontal lobe syndrome". This term is used as a descriptor of clinical presentation, rather than strictly denoting an underlying anatomical structure. After the advent of computerized tomography, it was observed that some lesions outside the frontal lobes, mostly confined to the subcortical structures, such as the thalamus and basal ganglia, could also result in frontal lobe syndrome.

A paradigm shift occurred in understanding the brain–behavior relationship within the last quarter of the 20th century. The centrist–localizationist approach gave way to the network approach, a new perspective that enabled the conception of discrete large-scale neurocognitive networks comprising cortical and subcortical components (1). At least two such networks subserving distinct executive and social cognitive functions are hosted by the frontal lobes (2). Based on current understanding, clinical neurology of the frontal lobes is parsed out as two subsyndrome: a dysexecutive syndrome associated with the dorsolateral prefrontal cortex and a disinhibited-social cognitive syndrome related to the orbitomedial prefrontal cortex (3). Herein, the author reports a case that not only presents two frontal subsyndromes concurrently but also a left-sided hemineglect following a right-sided striatocapsular infarction, thus illustrating how a relatively small subcortical area behaves as a bottleneck for the entire hemispheric cognitive functioning.

Case Report

A 70-year-old, right-handed woman with an elementary school education and a two-week history of behavioral change was brought to the author's attention in the neurology outpatient clinic. Her granddaughter reported a flu infection two weeks earlier with daytime sleepiness and a concurrent acute onset of behavioral change. She saw her family physician, who prescribed her an antihistamine and a non-steroidal anti-inflammatory drug for five days. The patient recovered from the flu infection within a week, but her behavioral changes and daytime sleepiness persisted.

The salient features of her behavioral change were loss of spontaneity, admixtured with restlessness, and an increase in appetite. She became reticent, almost unresponsive. The increase in appetite was particularly for sweets and manifested as late-night cravings. However, one morning she was found trying to eat a small plastic ball. When questioned, she replied: "these candies are not tasty anymore".

She had no other cognitive–somatic neurological symptoms. Her previous medical history included essential hypertension and idiopathic generalized epilepsy, which had been present since childhood. Reportedly, her seizure frequency had gradually subsided, decreasing to once every two years within the past 20 years. She had not had a seizure for at least one year. The drugs she used were listed as 10 mg of amlodipine once a day, 16 mg of candesartan once a day, 12.5 mg hydrochlorothiazide once a day, and 400 mg of carbamazepine twice a day. She had no history of cognitive impairment and was independent in her activities of daily living.

During the neurological examination, the patient was awake. Her apathy and perseverative behaviors were readily observable. She was indifferent, and her affect was blunted. She could not sit still on the chair, repeatedly stood up and wandered around the room, or displayed utilization behavior by manipulating various objects on the table. She had no sensory-motor neurological signs. Her mental status examination (MSE) comprised a short battery of bedside tests. The mini-mental state examination (MMSE) was used as a general cognitive screening test. The patient's score was 22/30, with a marked impairment in orientation to time and space. Luria's alternating series test, a bedside assessment of mental flexibility that comprises drawing alternating incomplete squares and triangles, revealed marked perseverations. The clock drawing test (CDT), which assesses several cognitive skills, including visuospatial functioning, abstract thinking, and planning, revealed left-sided unilateral neglect (Figure 1). The MSE was concluded with the frontal assessment battery (FAB) test, which includes six bedside tests for executive functions. Based on the FAB test results, the patient had difficulty comprehending similarities, reflecting impaired abstraction. Despite the repeated instructions reminding her of the rules, she kept recounting proper names in lexical verbal fluency (the second subtest). She was unable to perform Luria's alternating hand sequences (fist, palm, edge), another bedside test for mental flexibility (the third subtest). She showed complete insensitivity to interference by "conflicting instructions", which is the fourth subtest (i.e., "tap twice when I tap once"). She had no inhibitory control in the fifth subtest, the Go-No Go Task (i.e., "tap twice when I tap once, do nothing when I tap once"). Finally, she displayed environmental dependency in the sixth subtest, which focuses on prehension behavior (i.e., failure not to shake the extended hand of the examiner despite the explicit instruction: "do not take my hands"). Accordingly, she scored 0 on the FAB test. The total frontal behavioral inventory (FBI) is a 24-item questionnaire that assesses behavioral and personality changes via caregiver reports. It comprises a negative behavioral

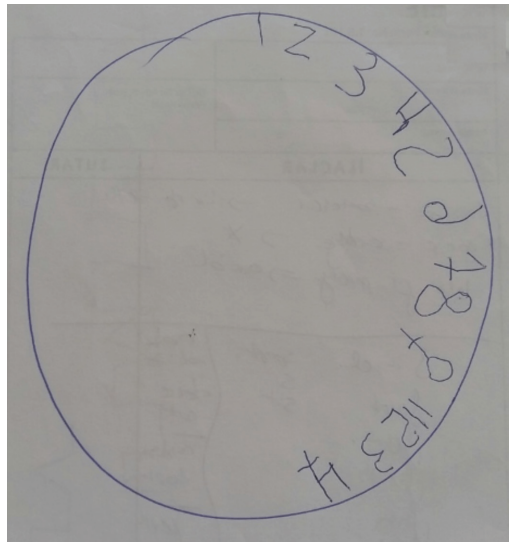

Figure 1. The clock drawing revealed unilateral neglect

score (NBS) and a disinhibition score (DS), with higher scores indicating frontal lobe dysfunction. The patient scored 31 (NBS: 23, DS: 8).

Routine laboratory investigations included a complete blood count, biochemistry (glucose, urea, creatinine, sodium, potassium, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase, amylase, total protein, albumin, chloride, calcium, magnesium, inorganic phosphorus, total bilirubin, direct bilirubin, creatine kinase, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, total cholesterol, triglycerides), thyroid function tests, ferritin, folate, and vitamin B12 levels, hepatitis markers, syphilis markers, anti-human immunodeficiency virus, chest X-ray, and an electrocardiogram. All results were within the normal range.

Brain magnetic resonance imaging (MRI) showed a large right-sided striatocapsular infarction, which included the head of the caudate nucleus, anterior limb of the internal capsule (ALIC), and anterior putamen (Figure 2).

The patient was diagnosed with probable vascular dementia (VaD) (according to the American Heart Association/American Stroke Association criteria) or major vascular cognitive disorder (following the Vascular Behavioral and Cognitive Disorders criteria) due to a strategically located cerebral infarction (4,5).

To evaluate the etiology of ischemic cerebrovascular disease, a transthoracic echocardiogram and Doppler ultrasound imaging of the carotid and vertebral arteries were performed. Her echocardiogram was normal. The Doppler ultrasound imaging showed atherosclerotic changes in the carotid arteries that did not cause significant stenosis. Subsequently, a computed tomography angiography of the cerebral arteries was performed, which showed atherosclerotic plaques without significant stenosis. The author prescribed the patient 300 mg of acetylsalicylic acid, once a day. The family was informed of a possible relative recovery over the following year and asked for follow-up visits.

The patient was brought back to the outpatient clinic ten months after the stroke. A family member noted that she had a daily intake of 7-8 liters of water. The polydipsia-associated low urine osmolality increased after fluid deprivation treatment. Her serum sodium level was 131 mg/dl. She spontaneously recovered from polydipsia within a few weeks.

The patient was reportedly better after one year at the routine follow-up examination. Her spontaneity had improved somewhat. She was calmer and displayed no bizarre eating behavior. Although still needing some prompting and instructions, she was able to manage some domestic chores. In her MSE, both scales sensitive to frontal lobe damage had improved: her FAB score had increased to 10, and her total FBI score had decreased to 7 (NBS: 7, DS: 0), which indicated a noticeable clinical improvement but not a complete recovery of frontal symptoms. Therefore, the author retained her previous diagnosis of VaD. The author ordered an ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) scan, which revealed large prefrontal hypometabolism, including all its subsectors (dorsolateral and orbitofrontal), as well as hypometabolism in the left cerebellar hemisphere (Figure 3).

Discussion

This is a case report of a female patient with an acute onset of frontal lobe syndrome and a left-sided hemineglect due to a right-sided striatocapsular infarction. The author used the MMSE, Luria's alternating series test, and CDT as general screening tools and the FAB and FBI for evaluating the frontal findings in detail. The FBI is a 24-item questionnaire that assesses behavioral and personality changes via caregiver reports, and the FAB is a group of bedside tests for executive functioning. The patient's cognitive status before the stroke was normal, as her relative stated that she had no history of cognitive impairment and was independent in her activities of daily living. The significance of her accompanying idiopathic epilepsy had apparently decreased over the years. The patient had no pyramidal findings, as the posterior limb of the internal capsule was spared, being located outside the vascular territory of the striatocapsular artery, in which pyramidal tracts travel through from the cortex.

The disconnection approach to the brain-behavior relationship was introduced by Norman Geschwind, the founding father of behavioral neurology (6,7). This approach was the culmination of observations indicating that the impairment of higher mental

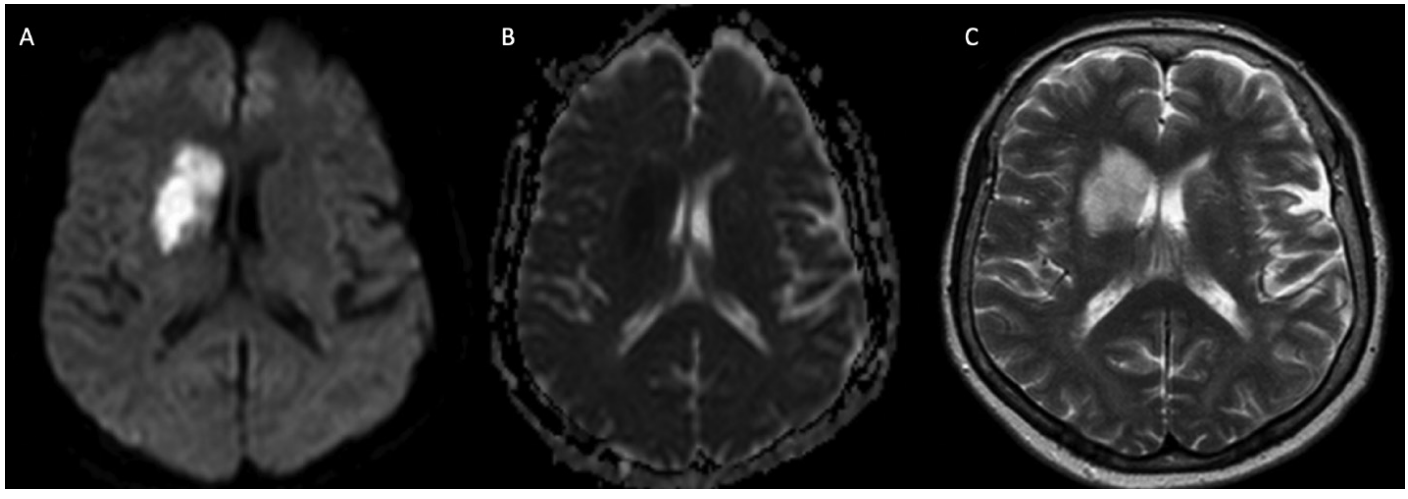

Figure 2. Magnetic resonance imaging shows an acute right-sided striatocapsular infarction. (A) Diffusion-weighted image. (B) Apparent diffusion coefficient image. (C) T2-weighted image

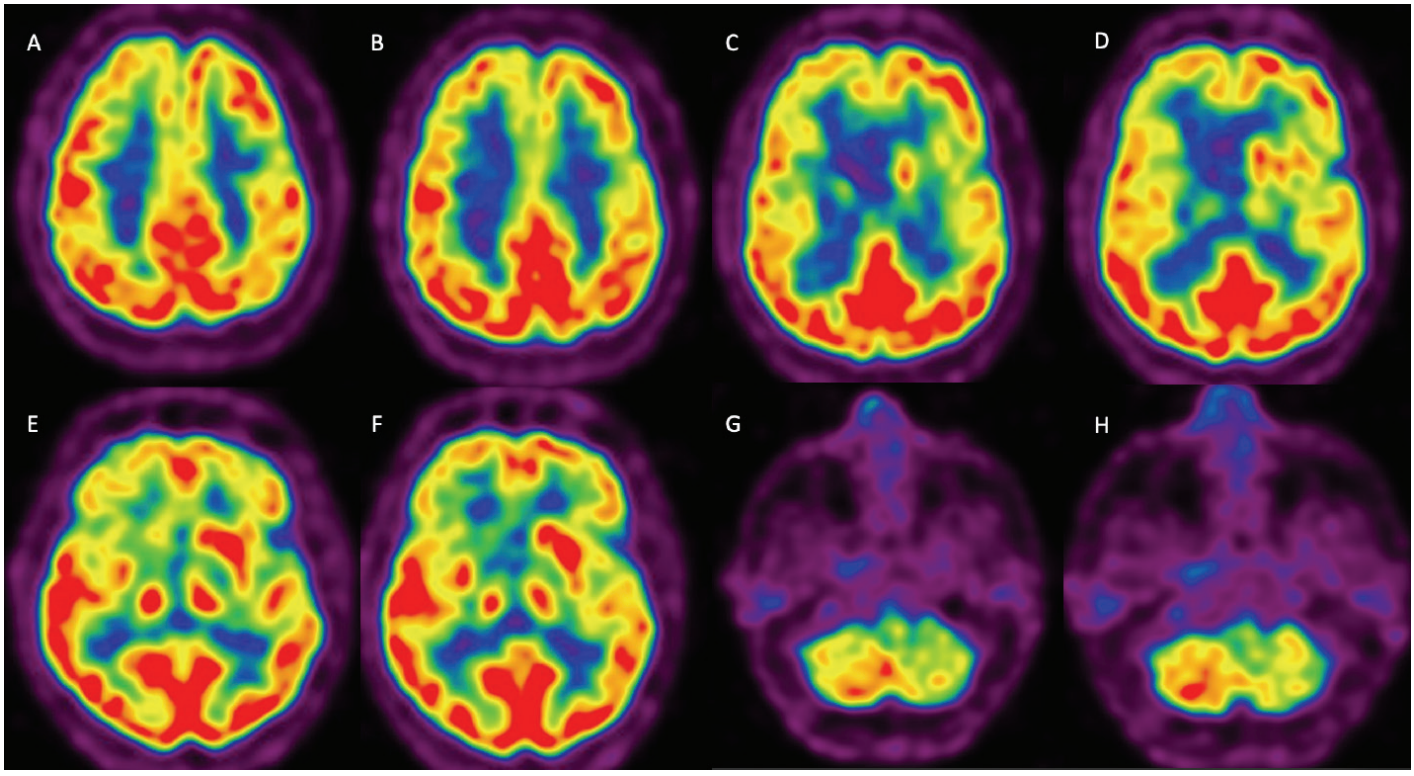

Figure 3. ^{18}F-fluorodeoxyglucose-positron emission tomography images showing right-sided prefrontal and left cerebellar hypometabolism. Note the asymmetrical metabolism pattern in the prefrontal subsectors and cerebellum: (A) frontopolar; (B) dorsomedial; (C, D) dorsolateral; (E) ventrolateral; (F, G) cerebellar

functions arises not only due to damage to the critical centers of the brain but also because of damage to the conduction pathways that interconnect these critical centers. The disconnection approach resulted in a paradigm shift in the understanding of the brain-behavior relationship; the centrist approach became outmoded and gradually gave way to the new paradigm, i.e., large-scale neurocognitive networks that comprise not only cortical hubs but also subcortical components, such as the association nuclei of the thalamus and different sectors of the dorsal and ventral striatal structures (1,8).

Five major frontal-subcortical circuits in the primate brain, defined by Alexander et al. (9), revolutionized the understanding of the basal ganglia. Following this historical paper, striatal structures other than the putamen, which are caudate with dorsolateral and ventromedial sectors, as well as ventral striatum, were associated with non-motor complex mental functions, such as executive control, social cognition, and reward-seeking. The five defined parallel circuits link specific frontal cortex regions, with a posterior-to-anterior gradient, to the specific regions in the basal ganglia and the thalamus and constitute a cortico-striato-pallido-thalamo-cortical closed-loop (2).

Recently Graff-Radford et al. (10) discussed in detail the cognitive and behavioral consequences of striatal lesions, such as apathy, loss of empathy, and hypersexuality, in two cases. Like the present case, the authors reported hypometabolism in the prefrontal cortex and contralateral cerebellum. The finding of ipsilateral frontal and contralateral cerebellar hypometabolism in the ^{18}F-FDG-PET scan demonstrates the widespread functional network disruption due to the relatively small-scale subcortical damage. Functional MRI studies have shown that the cerebellum contributes to executive control, the salience network, the default mode network, and to a lesser degree, the left frontoparietal network (11).

Mesulam et al. (12) suggested two models for the lesion-symptom relationship, one based on disconnection and the second on diaschisis. According to the disconnection model, a stroke lesion includes not only the cortex but also the deep white matter tracts, causing more deficits than the cortical lesion may do on its own. On the other hand, diaschisis refers to a change of function in a brain region that is not primarily damaged but has lost or decreased its function because it is critically connected to the distant and damaged brain area. Loss of function is not caused by simple disconnection (i.e., damage to the connecting pathway) but by a postsynaptic depression of neuronal activity due to loss of input (12). The most likely candidate for the underlying mechanism could be the diaschisis in the present study's patient.

The patient had a right striatocapsular infarct, which includes the ventral and dorsal caudate nucleus and the anterior putamen. While the ventral caudate plays a role in the emotional and affective aspects of behavior, such as reward processing, the dorsal caudate participates in cognitive and executive functions, such as spatial working memory. The anterior putamen has been attributed to social and language function, while the posterior putamen, which receives projections from the sensorimotor cortex, has been attributed to sensorimotor processing (10). This patient had no sensory-motor signs, and the posterior putamen was intact.

Having had a right-sided striatal infarction, including the anterior putamen, the patient had no aphasia, as would be expected from a left-sided striatal infarction, but displayed hemispatial neglect. The subcortical structures that partake in Mesulam's (1) definition of the large-scale distributed network for spatial attention are the medial pulvinar nucleus of the thalamus, striatum, and superior colliculus. Karnath et al. (13) subsequently reported that the putamen, the pulvinar, and, to a lesser degree, the caudate nucleus, are associated with spatial neglect. It can be suggested that the right anterior putamen, and likely the dorsolateral caudate nucleus, may be involved in spatial attention.

Acute confusion, abulia, loss of spontaneity, apathy, impulsivity, amnesia, aphasia, memory impairment, contralateral neglect, agitation, hyperactivity, depression, and hallucinations were reported as the clinical findings in acute caudate lesions (14,15). Although an abnormally increased craving for sweets has previously been reported for caudate nucleus lesions (10), to the author's knowledge, there has been no report concerning the mouthing of inedible objects, which was apparent in the current case in a very colorful way, almost similar to a Kluver-Bucy-like hyperorality.

The major limitation of this case report is the lack of resting-state MRI imaging (rs-MRI) data, which could directly support the above-mentioned network approach in terms of revealing dysfunctional intrinsic connectivity networks. However, it must be remembered that rs-MRI is still essentially a group comparison tool that is not undisputedly adapted for single-patient interpretation.

A partial hemineglect and apathetic-dysexecutive subsyndrome were evident in the present case. Although the patient was not overtly disinhibited, despite some purposeless hyperactivity and utilization behavior, hyperorality could be taken as evidence of a disinhibited social cognitive subsyndrome. The author suggests that the relatively small subcortical striatocapsular territory infarction, damaging the striatal structures and the ALIC, which carries the interconnecting and intersecting neural fibers of said neural circuit thus behaves like a bottleneck, could explain the full-blown right-hemispheric cognitive syndrome.

Ethics

Informed Consent: Patient consent was obtained.
Peer-review: Internally peer-reviewed.

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