

¹⁸F-fluorodeoxyglucose positron emission tomography and magnetic resonance imaging evaluation of chorea

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Abstract

Chorea is thought to be caused by deactivation of the indirect pathway in the basal ganglia circuit. However, few imaging studies have evaluated the basal ganglia circuit in actual patients with chorea. We investigated the lesions and mechanisms underlying chorea using brain magnetic resonance imaging (MRI) and ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET). This retrospective case series included three patients with chorea caused by different diseases: hyperglycemic chorea, Huntington's disease, and subarachnoid hemorrhage. All the patients showed dysfunction in the striatum detected by both MRI and FDG-PET. These neuroimaging findings confirm the theory that chorea is related to an impairment of the indirect pathway of basal ganglia circuit.

Introduction

Chorea is a hyperkinetic movement disorder characterized by brief, involuntary, and random muscle contractions. It occurs in several diseases and pathological conditions of the basal ganglia.¹ In the primate model of the basal ganglia circuit (Figure 1A), which consists of the direct and indirect pathways that start and stop movements, respectively, chorea is speculated to be caused by deactivation of the indirect pathway.^{2,3} However, few imaging studies have evaluated the basal ganglia circuit in actual patients with chorea. Here, we investigated the lesions and mechanisms underlying chorea in patients with three different diseases using brain magnetic resonance imaging (MRI) and ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Case Reports

Three patients with chorea due to different diseases treated at our hospital from 2013 to 2015 were included. We conducted brain MRI and FDG-PET studies in these patients. The experimental procedures used here were approved by the local ethics committee and were carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects.

FDG-PET studies were performed in the same method as previously described.⁴ Patients received an injection of FDG (185 MBq) in a resting state. They kept their eyes closed, and they relaxed in a dimly lit room for 60 minutes before being scanned with a whole-body PET/computed tomography (CT) system (Biograph 16; Siemens/CTI, Knoxville, TN, USA). All PET images were reconstructed using iterative algorithms (Fourier rebinding plus attenuation-weighted ordered-subset expectation maximization, with two iterations, eight subsets, and a 5 mm Gaussian filter) and CT-based attenuation correction. We calculated glucose metabolism in the striatum (putamen and caudate nuclei) and occipital lobes, and compared metabolic values of striatum with that of the ipsilateral occipital lobe. We defined the metabolic value of striatum (metabolism of striatum/metabolism of ipsilateral occipital lobe) as decline when it was 70% or less.

Case #1

A 90-year-old woman with poorly controlled diabetes mellitus presented with acute onset of hemichorea in her left face and left extremities. Her blood glucose level was 530 mg/dL, HbA1c was 14.5%, and ketosis was not present. Anti-glutamic acid decarboxylase antibody was positive, suggesting type 1 diabetes mellitus. On neurological examination, no abnormal findings were detected except for involuntary choreic movements. She was diagnosed with nonketotic hyperglycemic chorea. MRI of the brain showed T1 hyperintensity in the right basal ganglia (Figure 2A). FDG-PET demonstrated the decline of the metabolic value of the right striatum (Figure 2D). Oral haloperidol (1.5 mg/day) and subcutaneous insulin diminished her chorea after several weeks.

Case #2

A 36-year-old woman with Huntington's disease (HD) presenting with chorea in both upper extremities was admitted because of difficulty standing for one year. Her chorea had appeared eight years

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earlier, and she was diagnosed with HD 5 year prior. Genetic testing identified 47 CAG repeats in *HTT*. Brain MRI revealed diffuse atrophy in the cerebral cortex and caudate nuclei bilaterally (Figure 2B). FDG-PET showed a hypometabolic state in the bilateral striatum (Figure 2E). She was treated with tetrabenazine (12.5 mg/day), which relieved her chorea slightly.

Case #3

A 62-year-old woman with subarachnoid hemorrhage followed by vasospasm-induced right cerebral ischemia six years ago was admitted to our hospital for evaluation of involuntary movements, mainly in her neck, since the last ischemic attack. Neurological examination revealed complete paralysis of her left face and left extremities and detected large choreic

movements in her right sternocleidomastoid muscle (SCM) and small choreic movements in her right lower extremity. Brain MRI revealed T2 hyperintensity in the supplied area of right middle cerebral artery (Figure 2C). FDG-PET exhibited a hypometabolic state in the entire right hemisphere and the left striatum (Figure 2F) and increased glucose uptake in the right SCM and the right extremities (data not shown). Oral haloperidol (0.3 mg/day) alleviated her chorea after several weeks.

Discussion

We performed FDG-PET to evaluate chorea in three patients with different diseases. Deactivation of the indirect pathway of the basal ganglia is critical to the development of chorea,^{2,3} and we were able to characterize lesions in the basal ganglia in each patient.

FDG-PET revealed that the patient with hyperglycemic chorea (Patient 1) had hypometabolism in the right striatum (Figure 2D). In the previous papers,^{5,6} FDG-PET has revealed a hypometabolic state in the corresponding striatum or GP in patients with hyperglycemic chorea more than one month after onset. Our patient also underwent FDG-PET approximately one month after onset, and the results were consistent with the previous studies.^{5,6} Therefore, we suggest that the mechanisms leading to chorea in this patient included the decreased firing of the indirect pathway in the striatum, which inactivated the globus pallidus internus (GPi) and led to chorea as a result of hyperexcitability of the cortex and thalamus (Figure 1B).

In HD, the cerebral cortex and striatum are the most affected. The neurons in the striatum degenerate early in the disease course.⁷ The striatopallidal neurons in the indirect pathway are likely to be impaired in HD, which leads to the development of chorea.⁷ In a systematic review of FDG-PET studies in HD patients, several studies have demonstrated hypometabolism in the caudate nucleus and putamen.⁵ Our patient, Patient 2, had reduced glucose metabolism in the bilateral striatum (Figure 2E), suggesting that impairment of the indirect pathway caused her chorea (Figure 1B).

The patient with extensive lesions in the right hemisphere (Patient 3) developed chorea in the right SCM and lower extremity. FDG-PET demonstrated hypometabolism in the entire right hemisphere and the left striatum (Figure 2F). Whether ipsilateral, contralateral or bilateral cerebral cortex innervates the SCM remains controversial.^{8,9} This patient developed chorea in

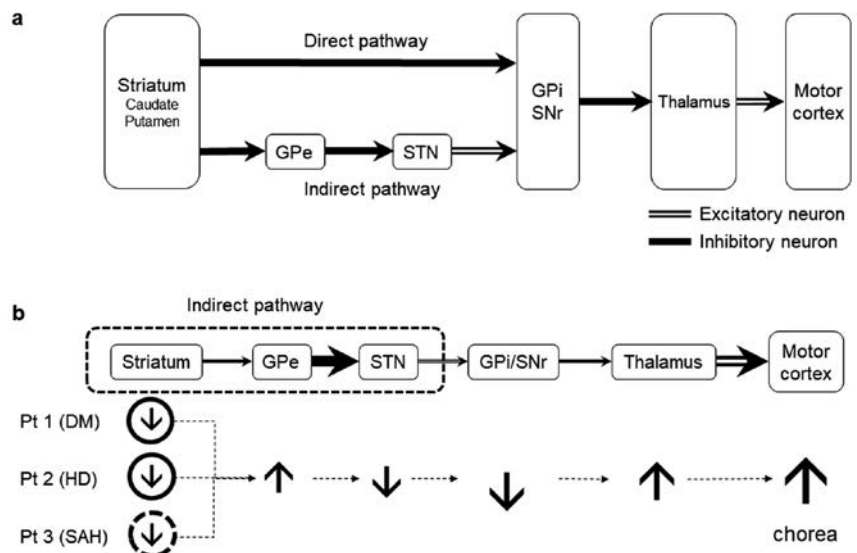


Figure 1. Schematic representation of the basal ganglia circuit and changes in activity of the basal ganglia components in the three patients. (A) The basal ganglia circuit consists of the direct and indirect pathways, which start and stop movements, respectively; (B) The activity of each component of the indirect pathway in the three patients changed as follows; patients 1, 2, and 3 had lesions in striatum, leading to GPi/SNr deactivation; deactivation of the GPi/SNr activated the thalamus, causing chorea. Arrows encircled by solid lines indicate primary lesions. The arrow encircled by a dashed line indicates a putative primary lesion. GPi, globus pallidus internus; GPe, globus pallidus externus; STN, subthalamic nucleus; SNr, substantia nigra pars reticulata; DM, diabetes mellitus; HD, Huntington's disease; SAH, subarachnoid hemorrhage.

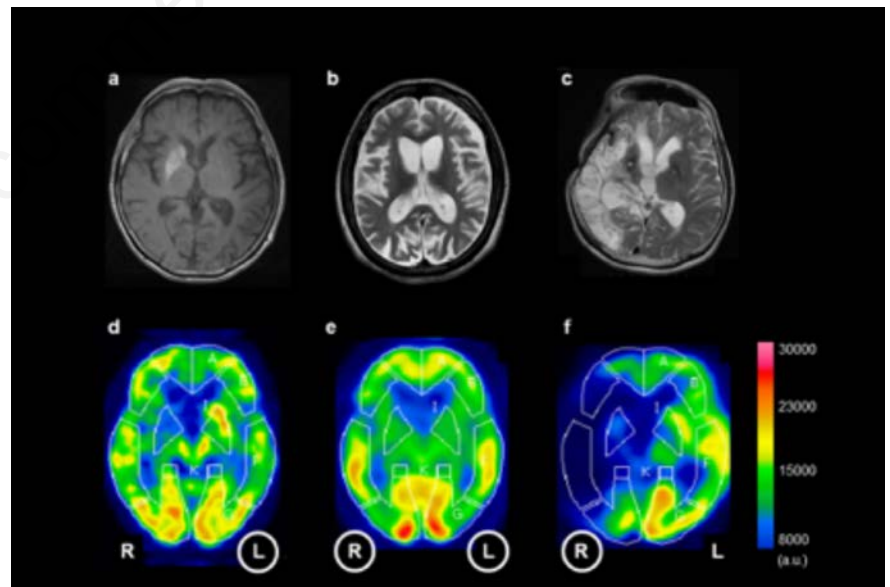


Figure 2. Brain magnetic resonance imaging (A-C). (A, Patient 1) T1 hyperintensity in the right basal ganglia (TR 756 ms; TE 9.7 ms); (B, Patient 2) Diffuse atrophy of the cerebral cortex and caudate nuclei bilaterally on T2-weighted images (TR 5,000 ms; TE 82 ms); (C, Patient 3) T2 hyperintensity in the supplied area of right middle cerebral artery. Brain 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) (D-F). (D, Patient 1) FDG uptake was reduced in the right striatum (right, 56% compared to that in right occipital lobe; left, 88%). (E, Patient 2) FDG uptake was reduced in the striatum bilaterally (right, 67%; left, 70%). (F, Patient 3) FDG uptake was decreased in the entire right hemisphere and the left striatum (left, 57%). The side of choreic movements was expressed as circled R (right) or L (left).

both the right SCM and the right lower extremity. Furthermore, her right motor cortex was damaged too severely. Thus, dysfunction of the left hemisphere led to chorea on the right, and deactivation of the left striatum might inactivate the indirect pathway, leading to her chorea (Figure 1B).

Conclusions

In all three patients, we did not detect any hypermetabolic state of the cortex or thalamus. This might be explained that patients relaxed for 60 minutes following FDG administration since during the relaxing time the choreic movement occurred only slightly.

This is the first study evaluating the mechanisms of chorea in actual patients using brain MRI and FDG-PET. Our neuroimaging findings confirmed the theory

that chorea is related to the impairment of the indirect pathway of basal ganglia circuit.

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