Evidence of thalamic disinhibition in patients with hemichorea: semiquantitative analysis using SPECT


Objectives: Hemichorea sometimes occurs after lesions that selectively involve the caudate nucleus, putamen, and globus pallidus. Some reports have hypothesised that the loss of subthalamic nucleus control on the internal segment of the globus pallidus, followed by the disinhibition of the thalamus may contribute to chorea. However, the pathophysiology is poorly understood. Therefore, clinicoradiological localisation was evaluated and a comparison of the haemodynamic status of the basal ganglia and thalamus was made.

Methods: Six patients presenting with acute onset of hemichorea were assessed. Neuroimaging studies, including MRI and SPECT examinations in addition to detailed biochemical tests, were performed. A semiquantitative analysis was performed by comparing the ratio of blood flow between patients and normal controls. In addition, the ratio of perfusion asymmetry was calculated as the ratio between each area contralateral to the chorea and that homolateral to the chorea. The comparison was made with a two sample t test.

Results: The causes of hemichorea found consisted of four cases of acute stroke, one non-ketotic hyperglycaemia, and one systemic lupus erythematosus. Brain MRI indicated lesion sites in the contralateral putamen, globus pallidus, caudate nucleus, and subthalamic nucleus. A significant decrease in the ratio of blood flow in the basal ganglia contralateral to the chorea and a significant increase in the thalamus was found when comparing the perfusion asymmetries, which were calculated as the ratio of cerebral blood flow (CBF) for each region to that in the homolateral occipital area (p<0.05).

Conclusion: An alteration in CBF in both the contralateral thalamus and basal ganglia reflect the loss of pallidal inhibitory input from the pallidum to the thalamus. This change in CBF may be one of epi-phenomena, which implicates an occurrence of hemichorea in humans.

SUBJECTS AND METHODS

Six patients (four men, two women) with an age range from 27 to 73 presented with hemichorea. Routine laboratory tests included the measurement of serum glucose, electrolytes, and urinary ketone concentrations. A brain MRI using a 1.5 Tesla superconducting system (Magnetom, Siemens) was obtained 3 days after onset of abnormal movement. The aetiologies of chorea in each patient were classified by laboratory and neuroimaging data. Another six age matched subjects without any other neurological diseases served as normal controls.

A brain SPECT was performed after intravenous injection of 740 MBq 99mTc HMPAO with lorazepam to reduce movement artifacts. However, the chorea was not completely abolished on examination. The data were obtained with a two head rotating gamma camera (MS II, Siemens, Germany) with a fanbeam collimator. A full 360° rotation was acquired with a

Abbreviations: CBF, cerebral blood flow; GABA, γ-aminobutyric acid; GPe, external globus pallidus; GPi, internal globus pallidus
matrix of 128×128, 10 mm thick axial slices, tilted along the orbitofrontal line, were reconstructed by a Butterworth filtered backprojection.

Analysis was performed both visually and quantitatively. Two experienced nuclear medicine physicians who were unaware of the patient’s clinical state, reviewed all the SPECT results.

**Semiquantitative analysis**

$^{99m}$Tc-HMPAO uptake in the basal ganglia, thalamus, cerebellum, frontal, parietal, temporal, and occipital area was quantified by placing appropriate regions of interest (ROI) on positions standardised under MRI guidance (fig 1). Two observers, blind to the clinical state, performed all quantitative analyses.

The analyses were performed by comparing the uptake in the region under evaluation with the uptake in a region unaffected by the disease. The occipital area was pathologically spared in the chorea and used as the referenced region. The CBF for each region was expressed as the ratio of HMPAO uptake in that region to that in the homolateral occipital area and the CBF ratios were compared between the patients with hemichorea and the normal controls. Additionally, the ratio of perfusion asymmetry was calculated as the ratio between each area contralateral and homolateral to the chorea. A comparison was made with a two sample $t$ test.

**RESULTS**

**Clinical and neuroimaging data**

Table 1 summarises the clinical, biochemical, and brain MRI results. The causes of the hemichorea found consisted of four patients with acute stroke (patients 2–5), one with nonketotic hyperglycaemia (patient 6), and one with systemic

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<th>4</th>
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<td>7</td>
<td>3</td>
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<tr>
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<td>HBP</td>
<td>DM</td>
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</table>

1. Left; R, right; P, putamen; C, caudate nucleus; GPi, internal pallidum; GPo, external pallidum; STN, subthalamic nucleus; NR, not recorded; NC, not checkable; SLE, systemic lupus erythematosus; HBP, hypertension; DM, diabetes mellitus.
lupus erythematosus (patient 1). Five patients (2–6) had a hemichorea involving the contralateral putamen, caudate nucleus, globus pallidus, and subthalamic nucleus. Patient 1, with systemic lupus erythematosus, had a hemichorea in the left limbs, but showed no definite anatomical lesion on brain MRI (fig 2 A and B). All patients received haloperidol (2–10 mg) and patient 1 was prescribed 60 mg oral prednisolone. The chorea subsided within 1–2 weeks after treatment.

Visual analysis
The brain SPECT showed a decreased blood perfusion of the basal ganglia and an increased perfusion of the thalamus contralateral to the choreic movement in all patients (fig 2 C). Patients 1, 3, 5, and 6 also had mildly decreased perfusion over the homolateral cerebellar hemisphere and patient 2 had increased perfusion over the right temporal region and patient 5 had decreased perfusion over the left parietal region. In the occipital area, no perfusion asymmetry was found. In addition, there was no perfusion defect in the controls.

Semiquantitative analysis
Table 2 summarises the blood flow ratios in the basal ganglia and thalamus referenced to that in the homolateral occipital areas. The means (SD) of the ratio in the basal ganglia and thalamus contralateral to the choreic movement were 0.88 (0.05) and 0.95 (0.06), respectively, and those for the region homolateral to the chorea were 0.97 (0.06) and 0.90 (0.06), respectively. By contrast with the patient group, the means (SD) of the right and left basal ganglia and thalamus blood flow in the controls were 0.98 (0.08), 0.96 (0.07) and 0.99 (0.03), 1.01 (0.03), respectively. When comparing the percentage of perfusion asymmetry with the normal controls, a significant decrease was found in the ratio of the flow of the basal ganglia contralateral to the chorea (p=0.014) and a significant increase was seen in the thalamus (p=0.001). However, there was no significant difference in the ratio of blood flow over the basal ganglia (p=0.074) and thalamus (p=0.218) contralateral to the chorea compared with that in the control group. Furthermore, no other CBF abnormalities were detected in the frontal, parietal, temporal, and cerebellar areas (p>0.05).

DISCUSSION
Experimental hemichorea models can be produced by injecting a γ-aminobutyric acid (GABA) antagonist into the external segment of the globus pallidus (GPe) or STN. The interruption of GABAergic transmission from the striatum to the GPe would lead to abnormally increased GPe neuron activity, which exerts inhibitory action on the STN. Increased STN inhibition would result in the loss of its control on the GPI. Besides excitatory STN inputs, the GPI neurons also receive inhibitory afferent inputs directly from the striatum. The imbalance between the indirect excitatory and direct inhibitory pathways ultimately leads to a disinhibition of the motor thalamus.

However, this simple pathophysiological model of the chorea has rarely been reported in humans. There are only two...
evaluated. In this case, lesions of the thalamus that only block the re-entrant influence of the basal ganglia, may leave intact those descending influences that are conveyed directly to the segmental motor apparatus.

Reports showing an increase in thalamic perfusion after a striatal ischaemic lesion\(^9\) or an increase in thalamic glucose metabolism in Huntington's disease.\(^6\) Moreover, there are observations that are difficult to reconcile with these simple models of basal ganglia function based primarily on the concept of thalamic disinhibition. One of the most noteworthy discrepancies involves the fact that lesions of the basal ganglia output nuclei do not result in dyskinesia.\(^7\) Another related problem in thalamic disinhibition theories is that lesions of the ventrolateral thalamus do not result in akinesia. Yet, according to such theories parkinsonian akinesia is generally attributed to increased basal ganglia outflow, which results in excessive inhibition at the ventrolateral thalamus level.\(^8\) One possible explanation for this apparent discrepancy is that the functional relevance of the descending basal ganglia outflow to the pedunculopontine nucleus may have been underestimated. In this case, lesions of the thalamus that only block the re-entrant influence of the basal ganglia, may leave intact those descending influences that are conveyed directly to the segmental motor apparatus.

Both SPECT and HMPAO were employed to obtain a functional status of the patients with hemichorea. Although a comparison of the ratio of blood flow over the basal ganglia and thalamus contralateral to the chorea with that in the control group was non-significant, our finding of perfusion asymmetry in the thalamus and the basal ganglia contralateral to the hemichorea was of particular interest because it may reflect the loss of pallidal inhibitory input to the thalamus. The CBF increase seen in the thalamus contralateral to the choreic movement probably reflects increased thalamic neuronal activity, free from inhibitory pallidal control. In addition, as seen in patient 1, a brain SPECT has many advantages over a brain MRI in detecting functional abnormalities in chorea. Because basal ganglia influence movement primarily through their projections to the primary or secondary areas of the motor cortex, some differences in cortical perfusion were seen in patient 1, a brain SPECT has many advantages over a brain MRI in detecting functional abnormalities in chorea.

### Table 2: SPECT findings for patient group

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<td>P6</td>
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<th>L PA/L PA</th>
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<td>0.94</td>
<td>1.00</td>
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</table>

| C1 | 0.93 | 0.98 | 0.92 | 0.81 | 0.74 | 1.06 | 0.97 |
| C2 | 1.14 | 1.13 | 1.02 | 0.94 | 0.91 | 1.04 | 1.01 |
| C3 | 1.13 | 1.08 | 1.01 | 0.87 | 0.79 | 1.06 | 0.96 |
| C4 | 1.05 | 1.03 | 0.97 | 0.83 | 0.83 | 0.95 | 0.92 |
| C5 | 0.88 | 0.86 | 0.99 | 0.75 | 0.75 | 0.97 | 0.97 |
| C6 | 0.95 | 1.01 | 1.02 | 0.77 | 0.85 | 0.98 | 1.08 |

1. left, R, right; BG, basal ganglia; TH, thalamus; CBL, cerebellum; OC, occipital area; FR, frontal area; PA, parietal area; TE, temporal area; L, T, decrease or increase in blood flow compared with contralateral side; NA, no asymmetry.
2. The ratio is expressed as the investigated regional blood flow for each region referenced to that the homolateral occipital area.

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mechanism concerning hyperkinetic disorders. However, the function of the thalamocortical projections and cortical areas, leading to chorea, remains unclear and some controversy still exists. Although our findings did not disclose the metabolic rate but the relative perfusion rate in the cortical area, this suggests that the chorea is produced by activation of an intact motor cortex by an abnormal or immature trigger pulse in the basal ganglia, which is in agreement with the original proposal by Kanazawa.22

Studying cortical metabolism in patients with hemichorea using positron emission tomography may be necessary.

We postulate that the primary event is a vascular insult in the striatum, leading to a dysfunction of the GABAergic projection neurons. Consequently, damage to the striatum that project through the GPi to the STN are selectively affected. In summary, our interpretation of the hyperperfusion of the thalamus found is in accordance with one of an ephiphenomenon, which implicates the occurrence of hemichorea in humans.

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REFERENCES
3 Martin TP, Akock NS. Hemichorea associated with a lesion of corpus lusii. Brain 1934; 57: 504–16.
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