Effects of Stereotactic Pallidal Surgery on Regional Cerebral Glucose Metabolism in Advanced Parkinson's Disease

IV. 9. Effects of Stereotactic Pallidal Surgery on Regional Cerebral Glucose Metabolism in Advanced Parkinson's Disease

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Introduction

Stereotactic pallidotomy has been established as an alternative treatment for advanced Parkinson's disease (PD)[1-4]. Although it is effective for relieving akinesia, tremor and rigidity, has also some risks of adverse effect such as dysfunction of higher brain functions, and bulbar palsy. In this study we evaluated changes in regional cerebral glucose metabolic rate (rCMRGlu) in PD patients using positron emission tomography (PET) before and after stereotactic pallidotomy. Correlations between rCMRGlu and clinical outcomes following the pallidotomy were also investigated.

Subjects and methods

Subjects

Three PD patients and 24 healthy volunteers participated in the study. The clinical characteristics of the patients are shown in Table 1. By Magnetic resonance (MR) imaging evident cortical or subcortical atrophy was not found both in patients and volunteers. All patients had quantitative PET 1 to 2 weeks prior to the pallidotomy and post-operative study was undergone after the operation. The protocol was approved by Clinical Committee of Radioisotope Use of this institution and all subjects gave their written informed consent for the study.

Positron emission tomography

The ^{18}F-fluorodeoxyglucose (FDG) PET was performed using Shimadzu HEADTOME-V scanner in 2-D data acquisition mode. A transmission scan was performed for attenuation correction of annihilation photons using a rotating 68Ge/68Ga line source. The subjects lay comfortably in the scanner bed and all studies were performed with their eyes close in a dim room and minimal auditory stimulation. 185 MBq in average of FDG was injected intravenously and 16 arterial blood samples were obtained for 50 minutes after the

tracer injection. Radioactivity of the plasma was counted with a well-type gamma counter to obtain a FDG input function. Cerebral glucose metabolic rate was calculated using the autoradiographical method scaned for 10 minutes beginning 40 minutes after injection. The lumped constant was 0.42 and the rate constants were as follows: k1=0.102, k2=0.130, k3=0.062, k4=0.0068.

Image analysis

To analyze focal metabolic changes between pre- and post- operative conditions, we applied a voxel-based statistical analysis using the Statistical Parametric Mapping (SPM99, Wellcome department of Cognitive Neurology, London) implemented on Matlab (Mathworks, Natick, Mass., USA)[5,6]. We defined the hypometabolic regions by comparing PET images of each patient over the Student's t-distribution obtained from 24 healthy normal volunteers adopting the statistical significance threshold at $p<0.001$ without correction for multiple comparisons.

Results

Case 1

Pre-operative PET study disclosed hypometabolic region mainly spreading over the prefrontal cortex corresponding to Brodmann area 9 and 10 (Fig. 1A). This patient underwent implantation of stimulator electrodes in the bilateral globus pallidus interna. Clinical performance assessed with Unified Parkinson Disease Rating Scale (UPDRS) revealed substantial improvement; from 51/100 at pre-operative state to 34/76 in stimulator-on condition. Two weeks after the operation, FDG PET in stimulating condition was performed. SPM analysis demonstrated a more intense and larger hypometabolic region in the prefrontal area (Fig. 1B). This patient's higher brain function assessed with WAIS-R and WMS-R revealed not-negligible deterioration after the operation.

Case 2

Pre-operative PET study of this case disclosed significant hypometabolic region over Brodmann area 39 and 40 which were considered to be strongly linked with association functions (Fig. 2A). This patient underwent left posteroventral pallidotomy (PVP). After the operation drug induced dyskinesia mainly in left side remarkably improved. But WAIS-R and WMS-R disclosed some impairment of intelligence as well as the bulbar palsy. SPM analysis demonstrated a newly developed hypometabolic region in bilateral prefrontal cortex; Brodmann area 9 (Fig. 2B).

Case 3

In case 3, PET study prior to the right PVP revealed no significant hypometabolic

region (Fig. 3A). The PVP could release the patient from severe wearing-off, akinesia and gait disturbance. However, impairment of general intelligence on WAIS-R and WMS-R appeared. Post-operative PET study demonstrated glucose hypometabolism in the right prefrontal cortex (Fig. 3B).

Discussion

PET has been established as the most useful method to evaluate the pathophysiological mechanism and quantitative evaluation of Parkinson's disease[7]. ^{18}F-fluorodeoxyglucose was applied to measurement of glucose metabolism in cerebral cortex and other deeply located structures such as globus pallidum, putamen and thalamus.

Previous PET study described that PD is associated with increased glucose metabolism in the thalamus and lentiform nucleus and decreases in the lateral frontal, paracentral, inferior parietal and parietooccipital areas. This metabolic profile has been showed to correlate with the disease progression as measured by the Hoehn and Yahr score[8]. Post-operative evaluation using FDG PET demonstrated that metabolic decreases in the thalamus ipsilateral to surgery site with increases in motor, premotor and supplement motor cortex (SMA) were correlated with the improvement of post-operative motor performance of the limb contralateral to pallidotomy. Furthermore post-operative hypometabolism in ipsilateral lentiform nucleus and the thalamus has been reported to have covaried with increases of glucose metabolism in bilateral SMA[9]. These findings are consistent with the basic concept involvement of the basal ganglia-thalamo-cortical circuitry and the theory that the pallidotomy effects result from artificial disruption of uncontrolled pallidal inhibitory output to the ventrolateral thalamus which consequently causes a reduced thalamocortical input and depressed cortical activity[7].

Previous report described that there was a greater risk of adverse effects such as cognitive and bulbar dysfunction after the pallidotomy, especially when employed to the bilateral targets[10]. From our cases, unilateral pallidotomy seems to have an enough potential to deteriorate higher brain function. FDG PET studies after the operation revealed the appearance of hypometabolic region in the prefrontal cortex bilaterally in case 1 and 2, and ipsilaterally in case 3. These metabolic reductions are a pathophysiological proof of the clinical adverse effects and presumably resulted from a functional disconnection of basal ganglia-thalamo-cortical circuitry as mentioned above.

We stress that the unilateral as well as the bilateral pallidotomy have a potential danger of deterioration of higher brain functions and this adverse effect can be functionally assessed by FDG PET.

References

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Table 1. Parkinson's disease patients undergoing stereotactic pallidotomy.

patient	age (yr)	sex	duration (yr)	surgery	Hoehn and Yahr stage		UPDRS	
					pre ope	post ope	pre ope	post ope
1	38	F	15	Blt. GPi stimulation	3/5	3/4	51/100	34/76
2	50	M	35	Lt. PVP	3/3	3/3	32/55	19/32
3	68	M	18	Rt. PVP	3/4	4/4	46/96	43/63

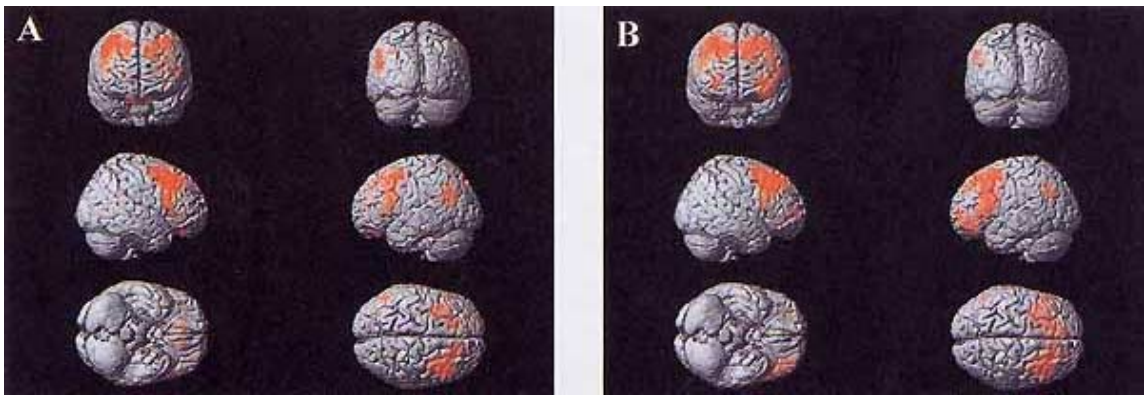

Fig. 1. Case 1. The glucose hypometabolic regions detected by SPM analysis are projected together onto a surface-rendered representative brain in standard stereotactic space ($p<0.001$, uncorrected for the multiple comparisons). (A) Pre-operative study revealed hypometabolism widely spreading over the lateral frontal lobe. (B) Post-operative study disclosed appearance of more intense and larger hypometabolism in the prefrontal area.

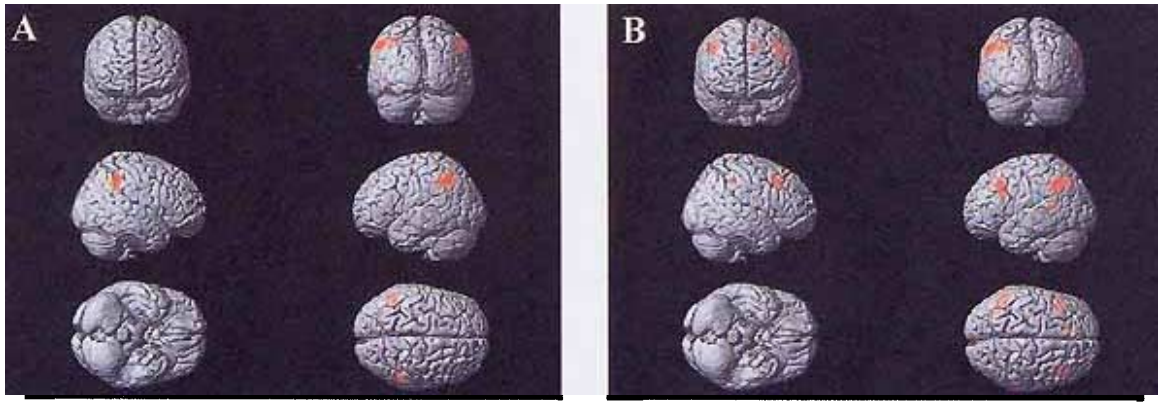

Fig. 2. Case 2. (A) Pre-operative study reveals hypometabolic region over Brodmann area 39 and 40. (B) After the operation SPM analysis of the FDG PET images discloses a newly developed hypometabolic region in bilateral prefrontal cortex; Brodmann area 9.

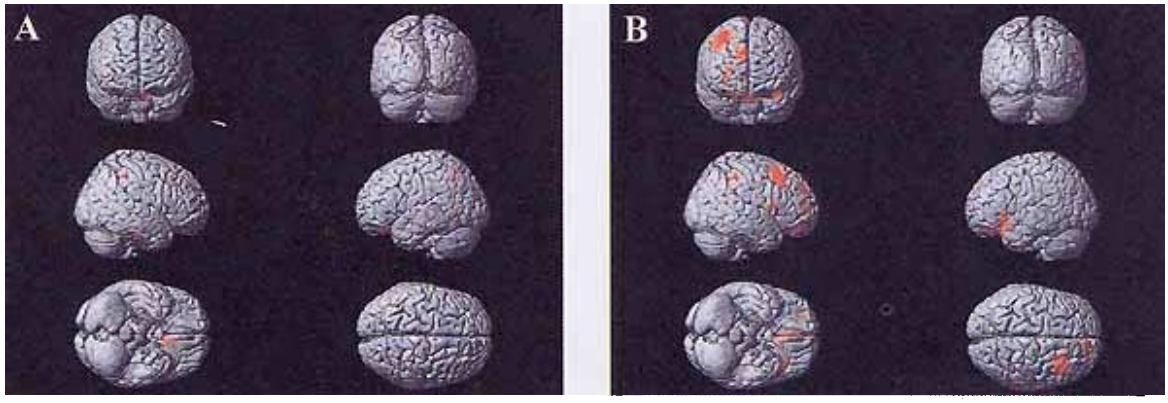

Fig. 3. Case 3. (A) SPM analysis does not detect significant hypometabolism before the operation. (B) Post-operative study reveals appearance of glucose hypometabolism in the right prefrontal cortex.