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Brain SPECT analysis by 3D-SSP and phenotype of Parkinson's disease

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Abstract

Objectives: We hypothesize that the regional pattern of blood flow reduction in the brain is different between tremor-dominant Parkinson's disease (PD) and postural instability gait difficulty (PIGD)-dominant PD. We therefore investigated the association of phenotypes in untreated PD with brain perfusion on SPECT using three-dimensional stereotactic surface projection (3D-SSP) technique.
Patients and methods: Thirty-three patients who had PD without dementia (12 men and 21 women with a mean age of 67.1 ± 6.4 years) were included in this study. Their symptoms were rated using the Unified Parkinson's Disease Rating Scale (UPDRS). Patients were grouped in two phenotypes: tremor and PIGD-dominant groups based on UPDRS components. Around the same time, all patients were examined by *N*-isopropyl-*p*[^{123}I] iodoamphetamine single photon emission computed tomography (^{123}I-IMP SPECT), and obtained images were analyzed with 3D-SSP using an image-analysis software, NEUROSTAT. Data on brain surface perfusion extracted by 3D-SSP analysis were compared between the PD patients and the normal control group. The same comparisons were made for subgroups of PD patients.
Results: Cerebral perfusion was decreased at the anterior cingulate cortex and primary visual cortex of the PD patients, and especially by the pixel-by-pixel comparison, perfusion was significantly decreased at the right anterior cingulate cortex compared with the normal controls. In the PIGD-dominant group, more severe hypoperfusion was seen at the same regions. In the tremor-dominant group, significant hypoperfusion was not seen compared with the normal controls.
Conclusions: The regional pattern of blood flow reduction in the brain was found to be different between tremor-dominant PD and PIGD-dominant PD. These regional differences were considered to suggest different and disease-specific combinations of underlying pathophysiological and neurochemical processes.

Keywords: Parkinson's disease; Unified Parkinson's Disease Rating Scale (UPDRS); PD phenotype; Tremor-dominant PD; Postural instability gait difficulty (PIGD)-dominant PD; Single photon emission computed tomography (SPECT); Statistical imaging technique; Three-dimensional stereotactic surface projection (3D-SSP)

1. Introduction

Because of recent progress in neuroradiological technology, it has become possible to assess cerebral function by computed tomography (CT) and magnetic resonance imaging (MRI), although these techniques have previously been limited to morphological data. However, the functions that can be detected by imaging are still limited to dynamic changes related to acute ischemia and the response of brain activity to testing. Usually, these methods cannot be used to detect a slow loss of neuronal activity due to cell degeneration and death. In contrast, brain single photon emission computed tomography (SPECT) can detect such changes at an early stage and will be able to visualize neurotransmission and receptor activity in the future. Changes of cerebral perfusion caused by diseases other than vascular injury are usually slight, however, leading to problems with the inter-reader precision and intra-reader reproducibility of SPECT. In addition, it is difficult to assess the three-dimensional size

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of a lesion by conventional SPECT. The statistical imaging method of brain SPECT was developed to solve these problems. Data obtained with a gamma camera are superimposed on a standard anatomical brain atlas, and are compared statistically on a pixel-by-pixel basis with the normal database. This makes it possible to visually evaluate abnormalities occurring outside vascular territories and to assess the association areas, both of which were difficult to evaluate by conventional tomographic methods. Several methods for the anatomic standardization of brain images have been developed, including statistical parametric mapping (SPM) [1,2], and three-dimensional stereotactic surface projection (3D-SSP) technique [3–5]. The 3D-SSP method has a particular advantage in the standardization of atrophied brain compared to SPM [6].

The clinical heterogeneity of idiopathic Parkinson's disease (PD) is well recognized. Besides the clinical variability between patients, the different parkinsonian features manifested by individual patients seem to progress at different rates, suggesting a variable involvement of the dopaminergic system and possibly other pathways. Furthermore it is well recognized that not all patients with PD respond the same way to levodopa treatment [7,8]. But to our knowledge, the relationship between brain perfusion and the clinical subtypes of PD have not been studied. We therefore investigated the association of phenotypes in untreated PD with brain perfusion on SPECT using 3D-SSP technique. Parkinsonian features were assessed by Unified Parkinson's Disease Rating Scale (UPDRS) scores, and patients were divided into two PD phenotypes [tremor-dominant or postural instability gait difficulty (PIGD)-dominant] based on various components of their scores. We hypothesize that the regional pattern of blood flow reduction in the brain is different between tremor-dominant PD and PIGD-dominant PD which suggests different and disease-specific combinations of underlying pathophysiological and neurochemical processes.

2. Patients and methods

2.1. Patients (Table 1)

Untreated PD patients without dementia who underwent brain SPECT in the Department of Neurology, Asahikawa Red Cross Hospital between March 30, 2001 and October 31, 2004 were included in this study. After patients with cerebral infarction, hypercapnia, and other diseases that may influence brain SPECT were excluded, as well as those who failed to satisfy the following SPECT criteria or posed certain technical problems, a total of 33 patients (12 men and 21 women), with a mean age of 67.1±6.4 years, were investigated. The diagnosis of PD was made according to the UK Parkinson's brain bank criteria [9]. They had suffered from PD for 1.6±1.8 years, and their mean Hoehn and Yahr [10] stage was 2.4±0.7. The Unified Parkinson's Disease Rating Scale (UPDRS) [11] scores were evaluated individually in all 33 patients. The mini mental state examination (MMSE) [12] revealed no mental deficits in any cases. Patients were placed in one of two groups, those with tremor-dominant PD and those with postural instability gait difficulty (PIGD)-dominant PD, as previously reported [13–15]. By this categorization, 10 patients were placed in tremor-dominant and 19 in PIGD-dominant group. Remaining 4 patients were not placed in both groups. Clinical features are summarized in Table 1. 17 age-matched volunteers were used as normal controls. They had no underlying diseases or impairment in the higher brain function, and were without abnormal findings in the brain except for those due to aging on MRI and MRA analysis. Informed consent was obtained from each subject.

2.2. Methods

2.2.1. Apparatus and materials

A gamma camera (GCA-9300API, Toshiba), an analytical workstation (GMS-5500/PI, Toshiba), and a Macintosh personal computer (PC) with Mac OS, and a Windows PC were used for data analysis. The software used for statistical analysis was NEUROSTAT [3–5].

2.2.2. Conditions for SPECT imaging and data acquisition

A dose of 222 MBq of ^{123}I-IMP was injected into a cubital vein (supine position, quiet surroundings, dimly lit room, eye closed), and scanning was done for 20 min from 10 min after injection. For each camera, the projection data were obtained in a 128×128 format for 30 angles in 120° increments at a rate of 40 s per angle. After correction for radiation scatter and absorption was done by the triple-energy window method [16] and by Chang's method [17], respectively, images were reconstructed. Regional cerebral blood flow was measured quantitatively using an arterial blood sampling method, modified by Kuhl et al. [18], which uses the microsphere model in all patients. Then the data were transferred to the PC through the network and 3D-SSP images were created with the image analysis program (NEUROSTAT).

2.2.3. Assessment

Nine cortical regions of interest (ROI) were predefined for each hemisphere using quantitatively analytical software, stereotactic extraction estimation (SEE) [19,20] which is an automated coordinate-based system to retrieve brain labels from the 1988 Talairach Atlas [21], as follows: lateral frontal association (including Brodmann's cortical areas, BA 6, 8–11, and 44–47); lateral parietal association (BA 5,7,39, and 40); lateral temporal association (BA 21,22,37, and 38); lateral occipital association (BA 18 and 19); medial frontal gyrus (medial part of BA 6); anterior cingulate (BA 24 and 32); posterior cingulate (BA 23 and 31); and primary visual cortices (BA 17); and cerebellar cortices. Cerebral blood flows were averaged between hemispheres, and there is no distinguishment between left and right in this analysis.