IV. 4. Assessment of Nigrostriatal Dopaminergic Function in Patients with Dementia with Lewy Bodies


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Introduction

Dementia with Lewy bodies (DLB) is characterized by progressive cognitive decline, extrapyramidal symptoms, episodic confusion, hallucinations and fluctuating cognitive impairment. Pathologically DLB is characterized by the presence of numerous Lewy bodies in the cortical and subcortical brain regions with variable Alzheimer-type pathology\(^1\). Recently it is suggested that DLB represents the second frequent cause of degenerative dementia in the elderly. The consortium on dementia with Lewy bodies (CDLB) proposed clinical diagnostic criteria of DLB\(^2\). However, some follow-up studies indicated a relatively poor sensitivity of the CDLB criteria to detect living DLB patients in contrast to an appropriate specificity\(^3\). This highlights a need to develop another clinical or laboratory diagnostic tool to provide a greater precision in the antemortem diagnosis of DLB. Since positron emission tomography (PET) using \(^{18}\)F-fluorodopa (FDOPA) provides a direct method of assessing presynaptic nigrostriatal dopaminergic function in living patients\(^4\), we analyzed FDOPA uptake with PET in the regions of caudate nucleus and putamen.

Subjects and methods

Ten patients with probable Alzheimer's disease (AD) (70.5±8.4 years, range: 58-86), seven patients with probable DLB (66.9±10.0 years, range: 51-79) and eight age-matched normal subjects were examined. All of the patients and the normal subjects were evaluated by medical and neurological examinations as well as by MRI to exclude other causes of dementia. The diagnosis of "probable AD" was established by the NINCDS-ADRDA criteria. We followed CDLB criteria for the diagnosis of probable and definite DLB. Normal subjects were all volunteers without any confirmed neuropsychiatric or major medical illnesses. The severity of dementia as assessed by Mini-Mental State Examination was not significantly different between DLB (15.7±6.7 points) and AD (16.3±5.0 points).

All subjects underwent PET scans using PT931 PET scanner (CTI, USA) with 7mm axial and transaxial resolution. Following an intravenous bolus injection of 2.5-8.3 mCi of
FDOPA, a series of 5 min emission scans was carried out for 60 minutes and emission data were simultaneously collected from seven contiguous axial sections. The tissue FDOPA concentration was measured by defining regions of interest (ROIs) on three image planes that included the caudate nucleus and putamen. ROIs in the caudate nucleus and putamen were defined on a summed image of data collected during the PET scan. An influx rate constant (Ki) of FDOPA into the selected regions was then calculated by the method described by Patlak et al.\textsuperscript{5} with radioactivity of the cerebellar hemisphere as an input function as described previously\textsuperscript{4}.

Results

In the DLB group, Ki values were significantly reduced in the caudate nucleus (0.0064±0.0017, p<0.001) and in the putamen (0.0051±0.0019, p<0.005) compared to the AD group (caudate nucleus: 0.0119±0.0021; putamen: 0.0092±0.0014). However, there was no significant difference in the Ki values between the AD and the aged normal group in either caudate nucleus or putamen (Figure 1). Using a cut-off value of 0.0062 (mean-2S.D. of the age-matched normal group) in the putamen, DLB could be distinguished from AD with a sensitivity of 86% and a specificity of 100% (For further details, see Ref. 6).

Discussion

According to the CDLB criteria, DLB patients are characterised by a variable combination of cognitive decline, parkinsonism and other symptoms. A considerable clinical heterogeneity or a complex array of the order of the onset of symptoms in DLB was documented in the literature. In this study, there was only a small overlap in the FDOPA-Ki values between the DLB group and the AD group, suggesting that nigrostriatal dopaminergic function using PET and FDOPA may be an informative diagnostic adjunct in distinguishing DLB from AD. Our observations are in good agreement with a series of pathological findings that there is a consistent loss of substantia nigra neurons and depletion of striatal dopamine content in DLB\textsuperscript{7,8}. Assessment of nigrostriatal dopaminergic function with PET and FDOPA alone or in combination with other PET images of glucose metabolism\textsuperscript{9,10} will help to improve sensitivity to detect living DLB patients so that these patients will benefit by an appropriate treatment during life.
References


Fig. 1 Individual influx rate constant (Ki) value of \(^{18}\text{F}\)-fluorodopa (FDOPA-Ki) in the caudate nucleus (O) and the putamen (Δ) in age-matched normal control (Aged Normal), Alzheimer's disease (AD), and dementia with Lewy bodies (DLB) are shown. Each bar represents mean Ki value. In the caudate nucleus, Ki values were 0.0129±0.0029 in aged normal, 0.0119±0.0021 in AD, and 0.0064±0.0017 in DLB. In the putamen, Ki values were 0.0114±0.0026 in aged normal, 0.0092±0.0014 in AD, and 0.0051±0.0019 in DLB. Statistical analysis was performed by one-way ANOVA.