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A follow up study of non-demented patients with primary visual cortical hypometabolism: Prodromal dementia with Lewy bodies

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ABSTRACT

We previously reported non-demented patients with glucose hypometabolism in the primary visual cortex (PVC), which is the preferentially affected region in patients with dementia with Lewy bodies (DLB). It remains unknown, however, whether these patients represent a prodromal DLB state. Eleven non-demented patients who attended our memory clinic for more than three years (mean follow-up period: 44 ± 5 months) were examined. All the patients had glucose hypometabolism in the PVC on [^{18}F]-fluoro-D-glucose (FDG) positron emission tomography (PET) scans at baseline. Four patients, including one with a clinical history of occipital bleeding, exhibited no core or suggestive features of DLB. Seven patients reported recurrent nocturnal dream-enactment behavior, which is consistent with probable rapid eye movement (REM) sleep behavior disorder (RBD). The condition of the patient with occipital bleeding was stable, which is consistent with an underlying non-neurodegenerative disorder. Of the remaining 10 patients, 5 had stable cognitive conditions (non-converters) and 5 exhibited progression to dementia (converters). The clinical diagnoses of 4 patients with probable RBD were changed to probable DLB. Despite no differences in psychological profiles at baseline between non-converters and converters, the initial pattern of cortical metabolism differed: converters had lower glucose hypometabolism in the parietal and the lateral occipital cortex compared to non-converters. The metabolic reduction in the PVC is present in patients with prodromal DLB. Moreover, the spatial profiles of reduced glucose metabolism at baseline could help to define the distinct prognostic subgroup that has a greater risk of conversion to DLB.

1. Introduction

Dementia with Lewy bodies (DLB) is the second most common neurodegenerative disorder after Alzheimer's disease (AD) in patients who attend memory clinics [1]. Accurate clinical diagnosis of DLB is important because of the differences in prognosis and management compared with other dementing disorders. Many previous longitudinal studies have revealed that specific patterns on neuroimaging and psychological testing in patients with mild cognitive impairment (MCI) predict progression to AD [2–4]. In contrast, there is little information regarding the specific patterns in patients with prodromal DLB [5–7]. This may be because clinical conditions corresponding to prodromal DLB have not been defined. Early differential diagnosis of DLB from AD is, however, important because several treatments with disease-modifying or neuroprotective potential in DLB are under investigation. It is extremely challenging to differentially diagnose DLB from AD in MCI patients.

Significant hypometabolism in the occipital cortex, observed on [^{18}F]-fluoro-D-glucose (^{18}F-FDG) positron emission tomography (PET) scans, particularly in the primary visual cortex (PVC), is considered to support a diagnosis of DLB [8]. We recently reported that some patients with glucose hypometabolism in the PVC who exhibit no dementia still have certain other clinical features of DLB, mainly recurrent nocturnal dream-enactment behavior, which is consistent with probable rapid eye movement (REM) sleep behavior (RBD) [9,10]. Dugger et al. reported that 60% of autopsy-confirmed DLB patients developed probable RBD before or during the year of estimated dementia onset, and thus some non-demented patients with probable RBD can convert to DLB [11]. It remains unknown, however, whether or not these non-demented patients in our memory clinic who have the metabolic pattern on ^{18}F-FDG PET scans represent the prodromal DLB state.

In this study, 11 non-demented patients with glucose hypometabolism in the PVC at baseline who visited our memory clinic were followed for more than 3 years. At baseline, four patients, including one with a clinical history of occipital bleeding, exhibited no core or suggestive features of DLB. Seven patients had probable RBD, which is one of suggestive features of DLB. During the observation period, the condition of the patient with occipital bleeding was

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stable, which is consistent with the theory that primary visual cortical hypometabolism is the result of a non-neurodegenerative disorder. Of the remaining 10 patients, 5 had stable cognitive conditions (non-converters) during the observation period and 5 exhibited progression to dementia (converters); the clinical diagnoses of 4 patients with probable RBD were changed into probable DLB. The purpose of this study is to report the first series of non-demented patients with glucose hypometabolism in the PVC who were followed in a memory clinic. We also compared the clinical profiles at baseline between converters and non-converters to define the distinct prognostic predictors that suggest the risk of conversion to DLB.

2. Methods

2.1. Patients and their clinical profiles at baseline

Eleven patients who were not demented at baseline (mean age: 70.9 ± 6.5 years; range: 60 to 80 years; 5 females and 6 males) and who visited our memory clinic at the Juntendo Tokyo Koto Geriatric Medical Center were followed for more than 3 years (mean follow-up period: 44 ± 5 months). All patients underwent ^{18}F-FDG PET scans at baseline between 2007 and 2009 at the PET/CT Dementia Research Center and showed glucose hypometabolism in the PVC (Fig. 1). Demographics and clinical profiles of these patients at baseline are summarized in Table 1. According to the clinical criteria of the Third Consortium on DLB (CDLB) [1], none of these patients exhibited the core clinical features of DLB at baseline. Seven of 11 patients reported recurrent nocturnal dream-enactment behavior, which is consistent with probable RBD, a suggestive feature of DLB [1,12]. The Mini-Mental State Examination (MMSE), the Wechsler Memory Scale—Revised (WMS-R), and the Wechsler Adult Intelligence Scale—III (WAIS-III) were used to assess cognitive ability. The motor subset of the Unified Parkinson's Disease Rating Scale (UPDRS) was used as an index of extrapyramidal motor signs [13]. Parkinsonism was considered to be present if any patient had a score of two or greater in at least two of the following cardinal features of Parkinson's disease: rigidity, bradykinesia, rest tremor, and postural instability [14]. The presence of visual hallucination was obtained from the patient and his or her informant via clinical interview every each visit. In 10 of 11 non-demented patients with glucose hypometabolism in the PVC, cardiac [^{123}I]-metaiodobenzylguanidine (MIBG) scintigraphy was also performed, as previously reported, to determine whether underlying Lewy body disease was present [15,16]. The heart to mediastinum (H/M) ratios for early and delayed images and the washout rate (WR) were calculated. Brain atrophy and/or

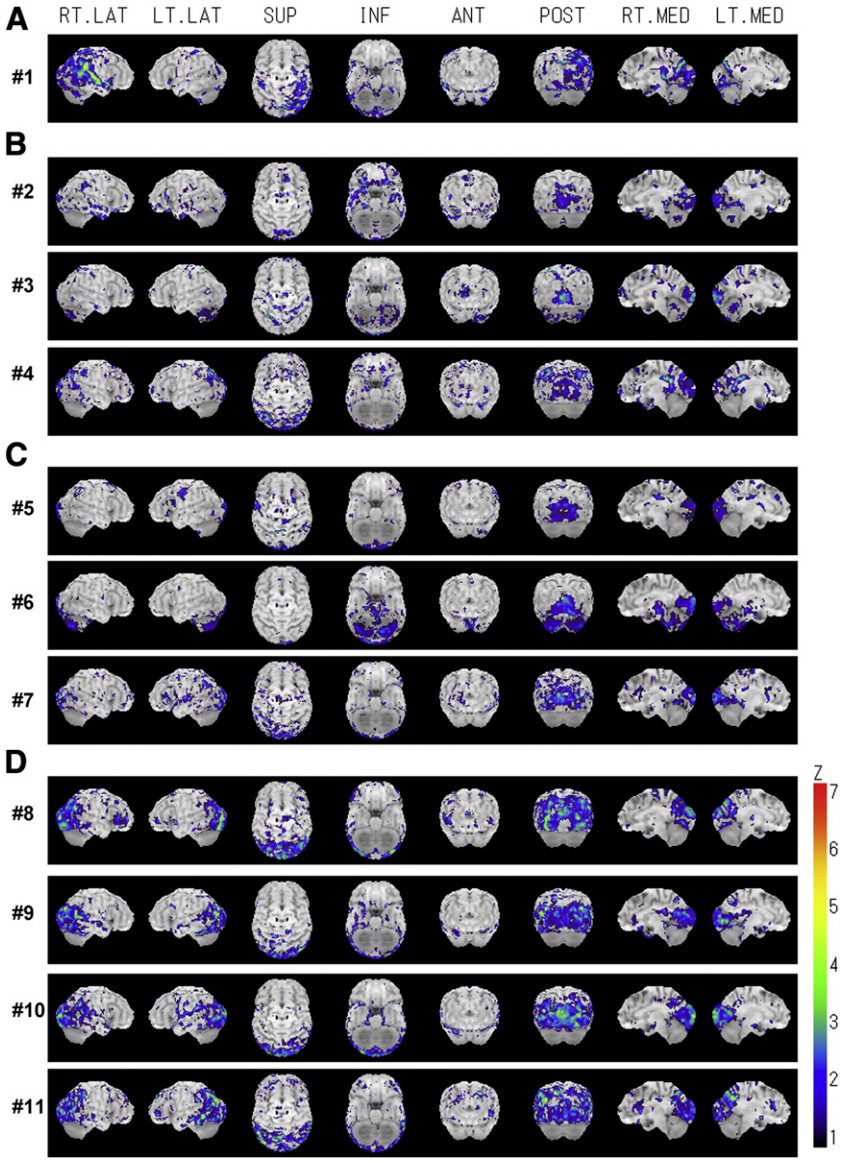

Fig. 1. [^{18}F]-Fluoro-D-glucose positron emission tomographic (^{18}F-FDG PET) scan results in non-demented patients with glucose hypometabolism in the primary visual cortex at baseline.