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Research article

The cingulate island sign in patients with dementia with Lewy bodies or Alzheimer's disease: A direct comparison between ^{18}F-FDG PET and ^{123}I-IMP SPECT

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ABSTRACT

The cingulate island sign (CIS) on ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET); i.e., the relative preservation of mid-posterior cingulate cortex metabolism, is a supportive biomarker in the diagnostic criteria for dementia with Lewy bodies (DLB). Information is lacking, however, regarding the diagnostic value of the CIS on FDG PET or ^{123}I-iodoamphetamine single-photon emission computed tomography (IMP SPECT) for differentiating between mild cognitive impairment (MCI) due to Alzheimer's disease (AD) (MCI-AD) and MCI due to DLB (MCI-DLB).

We examined the CIS ratio for nine AD patients, nine DLB patients, eight patients with MCI-AD, and nine patients with MCI-DLB using FDG PET and IMP SPECT. The CIS ratio was calculated as the total count density for the mid-posterior cingulate cortex divided by the total count density for the precuneus and cuneus using the stereotactic extraction estimation method. In the dementia groups, receiver operating characteristic analysis of the CIS ratio showed significant accuracy for differentiating between AD and DLB on both FDG PET and IMP SPECT. In the MCI groups, only the FDG PET-derived CIS ratio displayed significant accuracy for differentiating between AD and DLB. A larger study is needed to replicate these findings.

1. Introduction

Dementia with Lewy bodies (DLB) is the second most common form of neurodegenerative dementia after Alzheimer's disease (AD). The early differential diagnosis of dementia is important for care preparation, early life planning, and disease-modifying or neuroprotective treatment. Occipital hypometabolism (OHM) and occipital hypoperfusion (OHP), which can be detected using ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) or single-photon emission computed tomography (SPECT), are listed as supportive biomarkers for diagnosing DLB [1]. In the clinical setting, FDG PET and SPECT are frequently used not only for diagnosing AD and DLB, but also for differentiating these conditions from normal aging, frontotemporal lobar degeneration, corticobasal degeneration and so on. Moreover, SPECT is cost-effective and is more widely used than FDG-PET in many countries. Thus, obtaining evidence regarding the usefulness of FDG PET and SPECT for diagnosing DLB early would be valuable.

We previously reported the diagnostic value of FDG PET and ^{123}I-iodoamphetamine (IMP) SPECT focusing on the occipital region for differentiating between DLB and AD in patients in a demented state or with mild cognitive impairment (MCI) [2]. Recently, the FDG PET-based detection of the cingulate island sign (CIS); i.e., the relative

Abbreviations: AD, Alzheimer's disease; DLB, dementia with Lewy bodies; MCI, mild cognitive impairment; ^{18}F-FDG PET, ^{18}F-fluorodeoxyglucose positron emission tomography; ^{12}3I-IMP SPECT, ^{123}I-iodoamphetamine single-photon emission computed tomography; CIS, Cingulate island sign; OHM, occipital hypometabolism; OHP, occipital hypoperfusion; RBD, rapid eye movement sleep behavior disorder; MMSE, Mini-Mental State Examination; ROC, receiver operating characteristic; AUC, area under the curve

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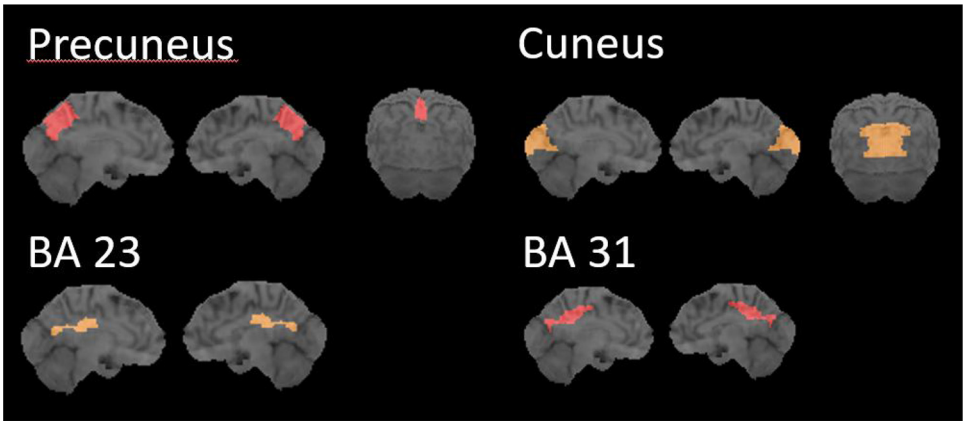

Fig. 1. Regions of interest in the precuneus and cuneus (Brodmann areas 23 and 31).

Table 1
Summary of the FDG PET- and IMP SPECT-derived CIS ratio data.

	Median CIS ratio of AD patients	Median CIS ratio of DLB patients	P-value	AUC	SE	95% CI	Optimal threshold	Sensitivity	Specificity
All patients									
FDG PET	0.370	0.417	< 0.0001	0.9314[a]	0.0392	0.8032–0.9783	0.3827	0.9444	0.7647
IMP SPECT	0.366	0.395[b]	0.0020	0.8072[a]	0.0755	0.6179–0.9155	0.3874	0.6667	0.8824
Difference				0.1242[b]	0.0616	0.0035–0.2449			
Dementia group									
FDG PET	0.363	0.402	0.0036	0.9136[a]	0.0656	0.6746–0.9818	0.3902	0.7778	0.8889
IMP SPECT	0.353	0.389	0.0062	0.8889[a]	0.0828	0.6073–0.9764	0.3774	0.7778	1.0000
Difference				0.0247	0.0682	−0.109–0.1583			
MCI group									
FDG PET	0.372	0.428	0.0018	0.9583[a]	0.0415	0.7500–0.9944	0.4094	0.7778	1.0000
IMP SPECT	0.378	0.402[b]	0.1358	0.7222	0.1368	0.4058–0.9082	0.3874	0.7778	0.7500

CIS, cingulate island sign; AUC, area under the curve; SE, standard error; CI, confidence interval.
[a] significant AUC.
[b] significant difference between FDG-PET and IMP-SPECT.

preservation of mid-posterior cingulate cortex metabolism, has been included as a supportive biomarker in the diagnostic criteria for DLB [1]. However, information is lacking regarding the usefulness of detecting the CIS on IMP SPECT for differential diagnosis in demented patients and regarding the usefulness of the FDG PET-derived and IMP SPECT-derived CIS for differential diagnosis in patients with MCI. Here, we calculated the CIS ratio, as the total count density for the mid-posterior cingulate cortex divided by the total count density for the precuneus and cuneus using the stereotactic extraction estimation method. We investigated the diagnostic usefulness of the CIS ratio using the retrospective data, and then receiver operating characteristic (ROC) analysis of the CIS ratio was performed in AD and DLB patients. After we had divided the patients into a dementia group and an MCI group according to their cognitive function, we performed the same analyses in these groups.

2. Method

2.1. Subjects

Thirty-five patients who visited the memory clinic at Juntendo Tokyo Koto Geriatric Medical Center from March to December in 2012 were examined. The subjects were described in detail in a previous study [2]. In short, they included nine AD patients (the AD group, mean age: 72.6 ± 8.5, male:female: 4:5), nine DLB patients (the DLB group, mean age: 76.3 ± 8.5, male:female: 6:3), eight patients with MCI due to AD (the MCI-AD group, mean age: 71.6 ± 5.7, male:female: 2:6), and nine patients with MCI due to DLB (the MCI-DLB group, mean age: 74.6 ± 5.6, male:female: 6:3). DLB was clinically diagnosed according to the 3rd edition of the DLB Consortium's diagnostic criteria for DLB [3]. AD was clinically diagnosed through clinical assessment mainly characterized by slowly progressive memory impairment according to the criteria developed by the National Institute on Aging and the Alzheimer's Association workgroup [4]. There were no significant differences between the demographics of the AD and DLB groups, or between the demographics of the MCI-AD and MCI-DLB groups. The mean Mini-Mental State Examination (MMSE) scores of the dementia groups (the AD and DLB groups) were ≤23 (19.3 ± 5.5 and 17.6 ± 4.0, respectively), and those of the MCI groups (the MCI-AD and MCI-DLB groups) were > 23 (26.3 ± 2.3 and 25.3 ± 1.0, respectively).

2.2. FDG PET and IMP SPECT procedures

All four groups were studied with ^{18}F-FDG PET and ^{123}I-IMP SPECT. The details of the ^{18}F-FDG PET and ^{123}I-IMP SPECT protocols were described elsewhere [2]. Regarding the CIS analysis, we calculated the CIS ratio in accordance with the method reported by Iizuka et al. [5] In short, the FDG PET and IMP SPECT images were fed into three-dimensional stereotactic surface projection software (iSSP installed in NEUROSTAT, AZE Ltd., Tokyo, Japan) to generate 3D cerebral metabolism/perfusion images [6]. We then applied region of interest (ROI) analysis to measure cerebral metabolism/perfusion using stereotactic extraction estimation software (SEE installed in NEUROSTAT, AZE Ltd., Tokyo, Japan) [7]. The mean regional count densities in each segment were automatically determined after segmentation based on the anatomical classification of the standard brain. The CIS ratio was calculated as the count density in the mid-posterior cingulate cortex (Brodmann areas (BA) 23 and 31; level 5 segmentation) divided by the count