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Basis of cingulate island sign may differ in dementia with Lewy bodies and posterior cortical atrophy

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Keywords

cingulate island sign; dementia with Lewy bodies; posterior cortical atrophy

With an increasing interest in the cingulate island sign (CIS) in dementia with Lewy bodies (DLB), and recently in posterior cortical atrophy (PCA), and with wider array of multimodality imaging methods, Drs. Kameyama and Iizuka outline the evolution of our understanding of the pathophysiology of CIS.

Kameyama and Iizuka comment on a recent study that showed substantially greater AV-1451 uptake across the entire cortical gray matter in patients with PCA compared to patients with probable DLB¹. Some DLB patients have additional Alzheimer's disease (AD)-related pathology and most PCA patients have AD as the underlying cause. However, we agree with Kameyama and Iizuka that both DLB and PCA often show relative sparing of the medial temporal lobe on MRI and a lower AV-1451 uptake in the medial temporal lobe on PET compared to the typical AD^{2, 3}. Preserved medial temporal lobe volume is associated with low degree of AD-related pathology in DLB and with atypical AD-related pathology distribution in PCA. In agreement with this atypical distribution, both PCA and DLB patients showed AV-1451 uptake in the occipital and posterior temporo-parietal cortices¹. However, the AV-1451 uptake, especially in the lateral occipital cortices, was substantially greater in PCA, and distinguished PCA from DLB with high sensitivity and specificity¹. More importantly, higher lateral occipital AV-1451 uptake also distinguished PCA patients with overlapping DLB-related features (REM sleep behavior disorder, visual hallucinations, parkinsonism or fluctuations) from DLB patients.

As Kameyama and Iizuka point out, PCA patients showed relatively lower AV-1451 uptake in the straight gyrus, medial orbitofrontal cortex, and the anterior cingulate cortex compared to the widespread uptake elsewhere¹. They interpreted the observation of relatively low AV-1451 uptake in these regions in PCA as a possible preservation of medial cholinergic pathway and may be the underlying pathophysiology for CIS on FDG PET. This may be true for PCA, and should be further investigated with AV-1451 and FDG PET in PCA patients. Conversely, DLB patients showed relatively higher AV-1451 uptake the straight gyrus, medial orbitofrontal cortices close to the basal forebrain nuclei, and in the anterior cingulate.

Thus, the basis of the CIS in PCA patients who likely have atypical AD pathology, and the CIS in probable DLB patients who likely have α -synuclein and a varying degree of AD pathology, may be different. CIS has been associated with low neurofibrillary tangle Braak stage⁴ and preservation of the medial temporal lobe volume⁵ in DLB patients. Moreover, recent study with a perfusion MRI using pseudo continuous arterial spin labeling sequence showed that CIS on arterial spin labeling MRI correlated with low medial temporal AV-1451 uptake in DLB patients⁶. Thus, these findings indicate that the posterior limbic network remains intact in DLB patients with low neurofibrillary tangle Braak stage, and CIS is lost with increasing neurofibrillary tangle Braak stage that leads to neurodegeneration in the medial temporal lobe and the posterior limbic network. Further research with an autopsy confirmation would lead to better understanding of the basis of CIS in both DLB and PCA patients.

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