Neuroimaging characterization of Psychiatric-onset prodromal Dementia with Lewy Bodies.

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Abstract

Objectives: Psychiatric-onset prodromal Dementia with Lewy Bodies (DLB) is a recently proposed clinical entity characterized by psychiatric presentation that may predate clinical dementia by many years. It is not yet clear how to identify patients with prominent late-onset psychiatric symptoms who may have underlying Lewy Bodies disease. Here, we describe how neuroimaging can assist the identification of this condition.

Methods: A 77-year-old man presented with late-onset psychosis. He underwent an extensive clinical and neuropsychological evaluation. These included Brain MRI with Arterial Spin labeling (ASL) which quantifies perfusion. $^{[123I]}$ FP-CIT SPECT and I-Metaiodobenzylguanidine (mIBG) scintigraphy assessed striatal dopaminergic and cardiac adrenergic integrity, respectively.

Results: Clinical evaluation revealed a history of REM sleep behavior disorder and parkinsonism induced by antipsychotics. The patient's cognitive function was normal. Conventional MRI showed parieto-occipital atrophy, and posterior hypoperfusion was revealed by ASL-MRI. Of note, the "cingulate island sign" was present. FP-CIT SPECT and I-Metaiodobenzylguanidine endorsed the suspicion of α-synucleinopathy. The patient fulfils the recently proposed key features of psychiatric-onset Prodromal DLB.

Discussion: Prodromal DLB is an emerging concept. Biomarkers have not been yet established. We propose that nuclear imaging and advanced MRI technics showing posterior hypoperfusion and the presence of the "cingulate island sign" could be promising biomarkers candidates.

A 77-year-old man, with no previous history of psychiatric disorder, presented with a 1-year history of recurrent and visual daytime hallucinations, some of which were very bizarre in content and unpleasant, including snakes crawling on the air conditioner, legless cats and dogs floating mid-air, children playing and people materializing from a water bottle and jumping out of the window, accompanied by the loss of insight. He had also a history of apathy and dream-enacting behaviour with vivid dreams. He underwent surgery for left retinal detachment three years before the onset of hallucinations, with normal vision post-surgery. No other general medical conditions were present, and no parkinsonism, cognitive decline or fluctuations were reported at that time. His family history was negative for neurodegenerative disorders. The patient was living with his spouse. His psychiatric history, including the presence of visual hallucination and apathy was obtained from unstructured interviews. A psychiatrist prescribed Olanzapine 5 mg and soon after, he developed marked parkinsonism. When he presented to our medical center, neurological examination revealed stooped posture, predominantly left-sided rigidity and bradykinesia. The patient scored 25/30 on the MMSE and extensive neuropsychological evaluation showed a normal cognitive profile, with no subjective cognitive decline and no fluctuations in cognition. $^{[123I]}$ FP-CIT SPECT demonstrated a bilateral dopaminergic nigrostriatal denervation with absent binding in the right putamen (**Figure 1**). Structural brain 3T MRI showed parieto-occipital atrophy. Arterial Spin Labelling (ASL)-MRI documented hypoperfusion in the parieto-occipital cortex with the evidence of the "cingulate island sign" (**Figure 2**). He has switched to quetiapine 25 mg with reduction in hallucination frequency. At 1-year follow-up visit, visual hallucinations were persisting. Follow-up neuropsychological evaluation confirmed a normal cognitive profile (MMSE score remained 25/30) and he continued to report no subjective cognitive decline. I-Metaiodobenzylguanidine (mIBG) scintigraphy showed postganglionic cardiac autonomic denervation and standard EEG diffuse theta slowing with and delta waves in fronto-temporocentral regions.

Discussion

We illustrated a case of late-onset psychosis in a patient with normal cognition who developed parkinsonism after the introduction of antipsychotic treatment. He presented well-formed visual hallucinations characterized the presence of complex narrative structure with images interacting and moving across the visual field with kinetic properties, thereby generating enriched scenarios. The initial diagnostic dilemma is to differentiate between the symptoms of psychosis due to a primary psychotic disorder versus psychotic symptoms that are secondary to neurological disorders. The phenomenology of the hallucinations, the presence of dream enacting behaviour with vivid dreams suggestive of rapid eye movement sleep behavior disorder (RBD) and the presence of apathy raised the suspicion of an α-synucleinopathy. However, the time-course consistent development of parkinsonism following treatment with a dopamine receptor blocker argues against a diagnosis of Parkinson Disease (PD).[1] Furthermore, well-formed visual hallucinations are uncommon in the early stages of PD. [2,3] On the other hand, the diagnosis of Dementia with Lewy Bodies (DLB) cannot be considered as dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities, is an essential requirement for DLB diagnosis.[4]

However, some studies show that neuropsychiatric symptoms, such as hallucination and apathy, can be identified in cognitively-preserved patients many years before the diagnosis of DLB.[5,6] Of note, research criteria for the diagnosis of prodromal DLB have been recently proposed.[7] Psychiatric-onset Prodromal DLB is characterized by predominant psychiatric symptoms, which may feature hallucinations in visual and in other modalities, and systematized delusions. Proposed key features included apathy and parkinsonism that may be induced by antipsychotic medications used to treat psychiatric disorder.[7] Considering the clinical features, including RBD, and the neuroimaging findings highly suggestive of α-synucleinopathy, our case fit this recently proposed criteria for psychiatric-onset Prodromal DLB.

Biomarkers for psychiatric-onset DLB have not been yet established, however, it could be assumed that they are similar to those identified in DLB.[7] Reduced dopamine transporter uptake in basal ganglia and reduced mIBG uptake demonstrated on myocardial scintigraphy are current indicative biomarkers in DLB, while low occipital uptake on perfusion/metabolism scan constitutes a supportive biomarker for this diagnosis.[4] The "cingulate island sign" characterized by relative preservation of posterior cingulate relative to the precuneus plus cuneus metabolism on FDG-PET, has been described in DLB,[4] however, this value has not been established in predementia stages and using perfusion imaging such as ALS-MRI. This case highlights that imaging biomarkers could be considered in patients developing late-onset psychiatric disease, especially when other clinical features of synucleinopathy are present. Further prospective investigations are required to clarify the role of these biomarkers and to guide the construction of formal criteria for psychiatric-onset prodromal DLB.

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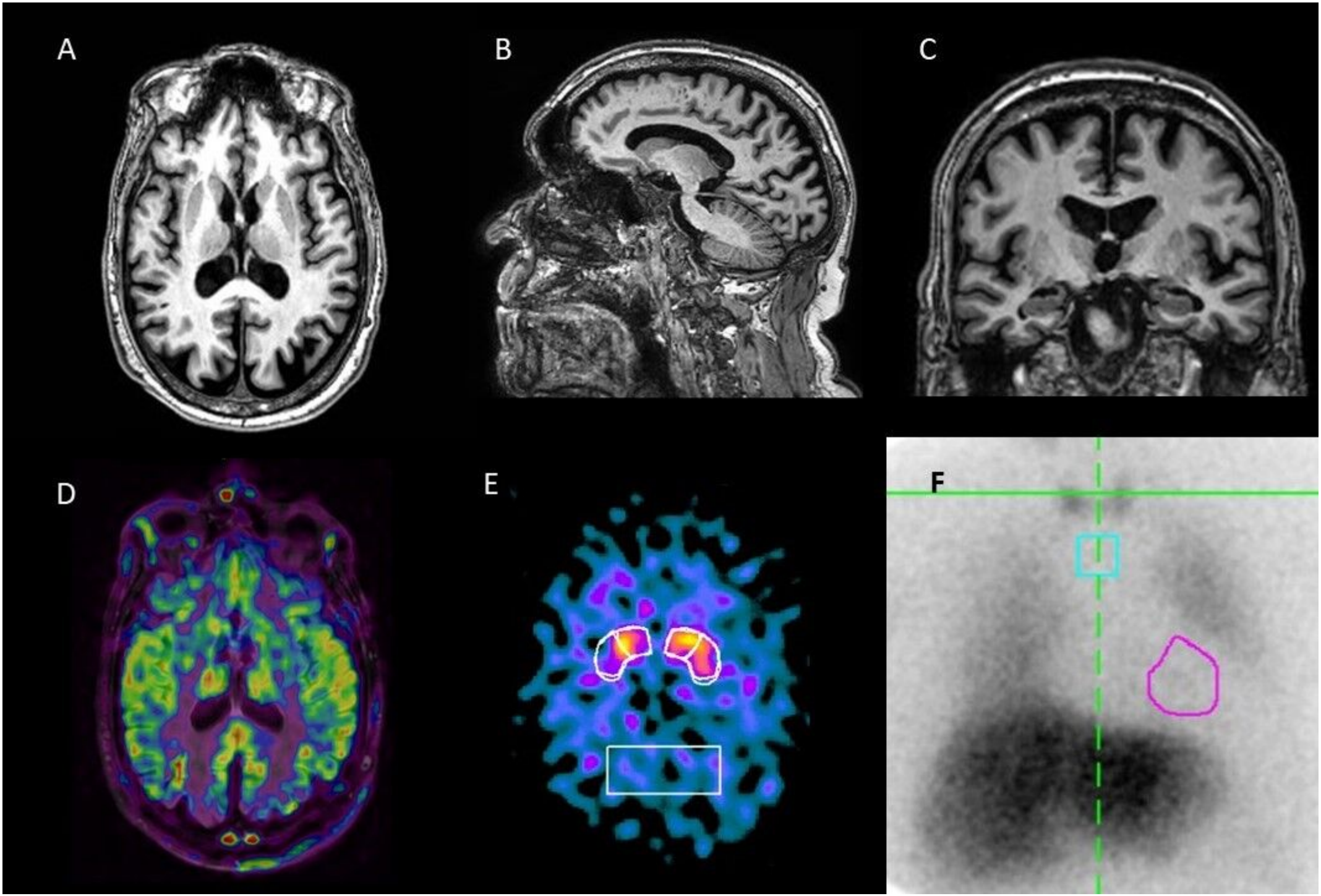
Figures

Figure 1: Neuroimaging findings in a case of psychiatric-onset prodromal DLB.

Axial T1-weighted and sagittal T1-weighted brain MRI sequences show parieto-occipital atrophy, particularly in the cuneus and the precuneus regions, with preservation of anterior structures volumes (A-B). Coronal T1-weighted brain MRI, show the relative preservation of medial temporal lobe volume (C). Arterial Spin Labelling (ASL)-MRI documented parieto-occipital hypoperfusion with relative preservation of other brain regions (D). $^{[123I]}$ FP-CIT SPECT showed a reduced bilateral dopamine transporter uptake in the striatum with absent binding in the right putamen (E). I-Metaiodobenzylguanidine (mIBG) myocardial scintigraphy images taken 3 hours after injection demonstrated postganglionic sympathetic cardiac denervation (F). Typical regions of interest are shown on the left hearth ventricle (circumscribed by the violet line) and upper mediastinum (light blue square). The method of imaging investigations was qualitative for MRI (A-D) and quantitative for [123I] FP-CIT SPECT and mIBG (E,F)

Figure 2: The "cingulate island sign".

Arterial Spin Labelling (ASL) MRI standard axial view transecting the posterior cingulate region in healthy control (A) and psychiatric-onset Prodromal DLB (B). The “cingulate island sign” is characterized by relative preservation of posterior cingulate relative to the precuneus plus cuneus on metabolism or perfusion imaging. In the healthy control, ASL-MRI signal is normal in the posterior cingulate, occipital, and other neocortical regions (A). Our patient had normal perfusion in the posterior cingulate region (red arrow) surrounded by visually reduced ASL perfusion in the adjacent occipital cortex, representing the cingulate island sign (B).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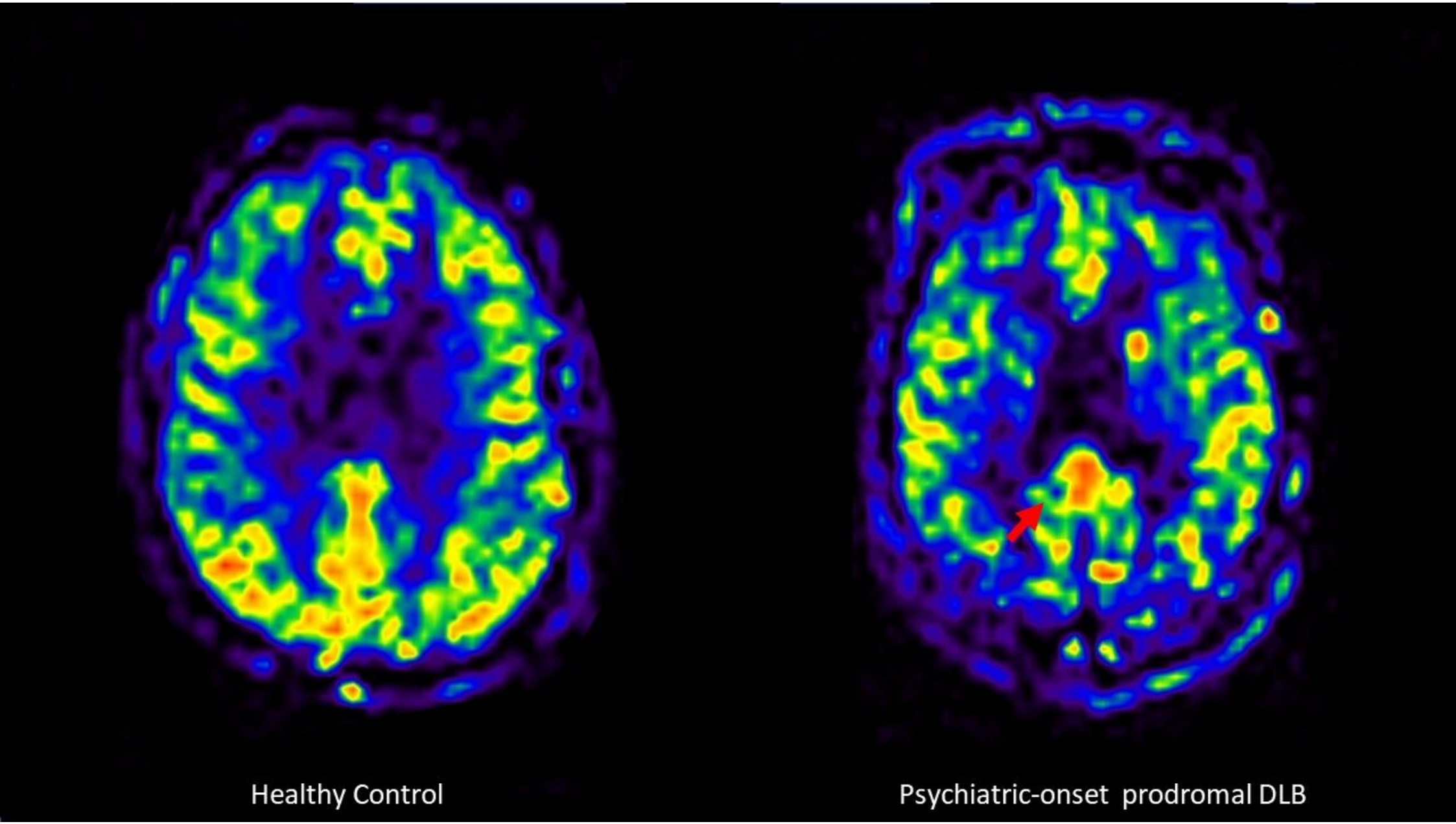
Healthy Control
Psychiatric-onset prodromal DLB