

# Brain Metabolic Heterogeneity in Corticobasal Syndrome (CBS): Dissociation from Amyloid and Tau Pathology *in vivo*

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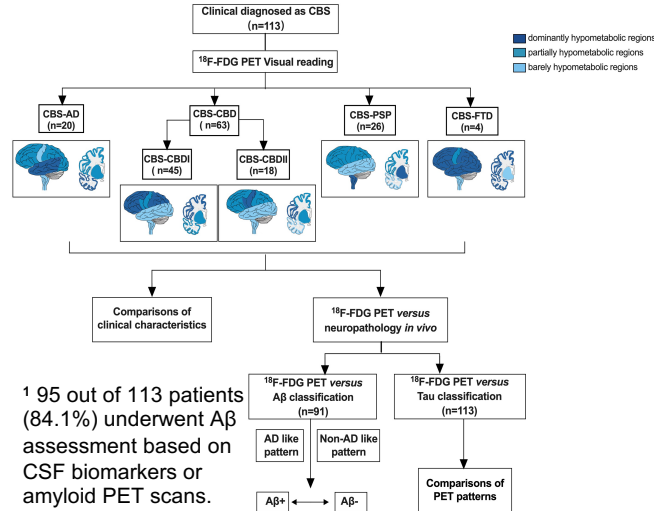
## Background

Previous neuropathologic studies have revealed heterogeneous underlying pathologies of CBS, including 4R tauopathies, CBD and PSP, together accounting for two-thirds of cases, and AD as the third most common pathology. However, it remained unclear whether a single pre-established FDG PET could predict A and T statuses in CBS patients.

## Methods

113 patients clinically diagnosed as CBS were recruited from Dec 2019 to Feb 2025 at the Movement Disorders Clinic, Department of Neurology, Huashan Hospital, Fudan University (Shanghai, China). The study flowchart was presented in **Figure 1**. According to the heterogeneous patterns of FDG PET, patients with CBS were divided into CBS-AD, CBS-CBD, CBS-PSP and CBS-FTD.

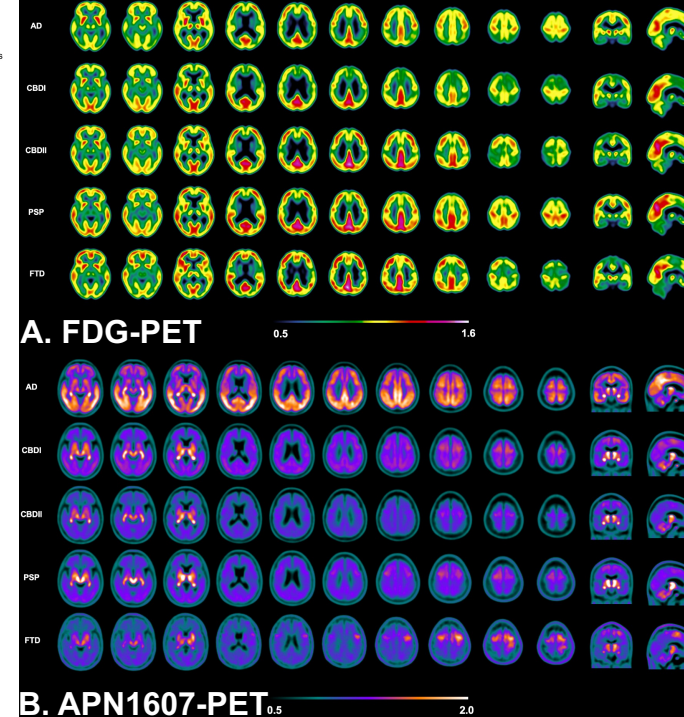
**Figure 1. Flowchart**



## Results

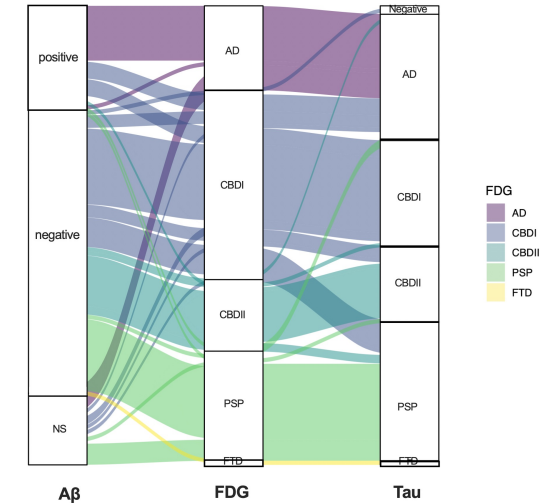
Two distinct types of CBS-CBD were further classified as peripheral type-I (decreased metabolism originated from frontal and parietal cortices to the central sulcus, with internal frontal cortex and SMA mostly involved) and central type-II (decreased metabolism originated from PMA and M1 regions around the central sulcus to frontal and parietal cortices), as **Figure 2A** shown.

**Figure 2. Group-wise PET images**



Although CBS-AD, CBS-CBDI, CBS-CBDII and CBS-PSP exhibited comparable disease severity, patients with CBD-CBDII showed relatively preserved cognitive function. The **Figure 2B** displayed the group-wise  $^{18}\text{F}$ -Florzolotau PET SUVR imaging across different subgroups, as divided by FDG patterns.

**Figure 3. Comparisons of FDG-PET patterns vs A $\beta$  and Tau pathology *in vivo***



The AD metabolic pattern showed high specificity for amyloid  $\beta$  positivity (98.5%) and for combined AD pathology (amyloid  $\beta$  plus tau, 98.6%), with correspondingly lower sensitivity (54.2% and 72.2%).  $^{18}\text{F}$  FDG PET patterns further showed high specificity for the PSP tau profile (96.2%) and high sensitivity for the CBD tau profile (97.7%).