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PET imaging of synaptic health in syndromes associated with frontotemporal lobar degeneration

The clinical and pathological heterogeneity across the spectrum of frontotemporal lobar degeneration is a challenge for diagnoses and experimental medicine, calling for efficient biomarkers to stratify and monitor in clinical trials. Loss of synapses and their plasticity is an early and clinically-relevant feature of frontotemporal dementia and related disorders. Positron emission tomography (PET) can be used to measure synaptic health and function. From early work with FDG to novel PET ligands for synaptic vesicle glycoprotein 2A, in vivo PET has been crucial to quantify and localise synaptic dysfunction. The combination of PET markers for synaptic health, with physiological and fluid markers of other pathological processes, offers fundamental insights into frontotemporal dementias, and provides biomarkers with clinical utility. These tools can facilitate the validation of preclinical models, and inform the design of new disease-modifying treatment strategies.

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