The pathologic hallmarks of Alzheimer’s disease (AD) include abnormal deposits of extracellular beta amyloid plaques and aggregates of hyperphosphorylated tau neurofibrillary tangles (NFTs). Current evidence strongly supports the role of beta amyloid as a disease initiating event occurring years before symptom onset. NFT accumulation has been thought to follow beta amyloid by 5-10 years. While beta amyloid has been associated with cognitive decline, the relationship between cortical beta amyloid and clinical disease stage has not been consistently supported. In contrast, the accumulation of tau is more closely associated with the degree of cortical neuronal loss as well as with increasing cognitive deficits and declining functions of daily living. Autopsy findings have indicated stronger correlations between NFT number and pre-mortem cognitive performance than counts of beta amyloid plaques in those same individuals. Across a substantial body of literature tau pathology has also been shown to be more closely related to cognitive impairment, predominantly memory decline, than amyloid in postmortem studies.

The advent of molecular imaging agents providing quantitative measures of beta amyloid and tau have allowed researchers to explore these proteins in AD in vivo. Therapeutic trials now routinely employ molecular imaging to screen prospective subjects as a component of enrollment criteria and to monitor response to therapy occurring at the cellular level. The relationship between tau tracer PET signal and cognitive performance has also been explored, though results have varied across studies, with most studies reporting substantial and significant correlations between neocortical tau standard uptake value ratios and Mini-Mental State Examination. Based on the neuropathological literature and early PET studies, it appears that the spatial location and density of tau may be indicative of the degree of neurodegeneration, synaptic dysfunction, and the character of cognitive deficits. Thus we hypothesized that the density and distribution of pathological tau (measured by PET imaging of Flortaucipir F 18) would correlate with cognitive impairment across a range of domains in a regionally distinct manner. This preliminary work explores relationships between spatial distribution of flortaucipir and a range of cognitive functions as assessed by neuropsychological measures.