

Longitudinal Relationships Between Amyloid Accumulation, Cognitive Decline, And Head-To-Head Changes In Flortaucipir And MK6240 Uptake

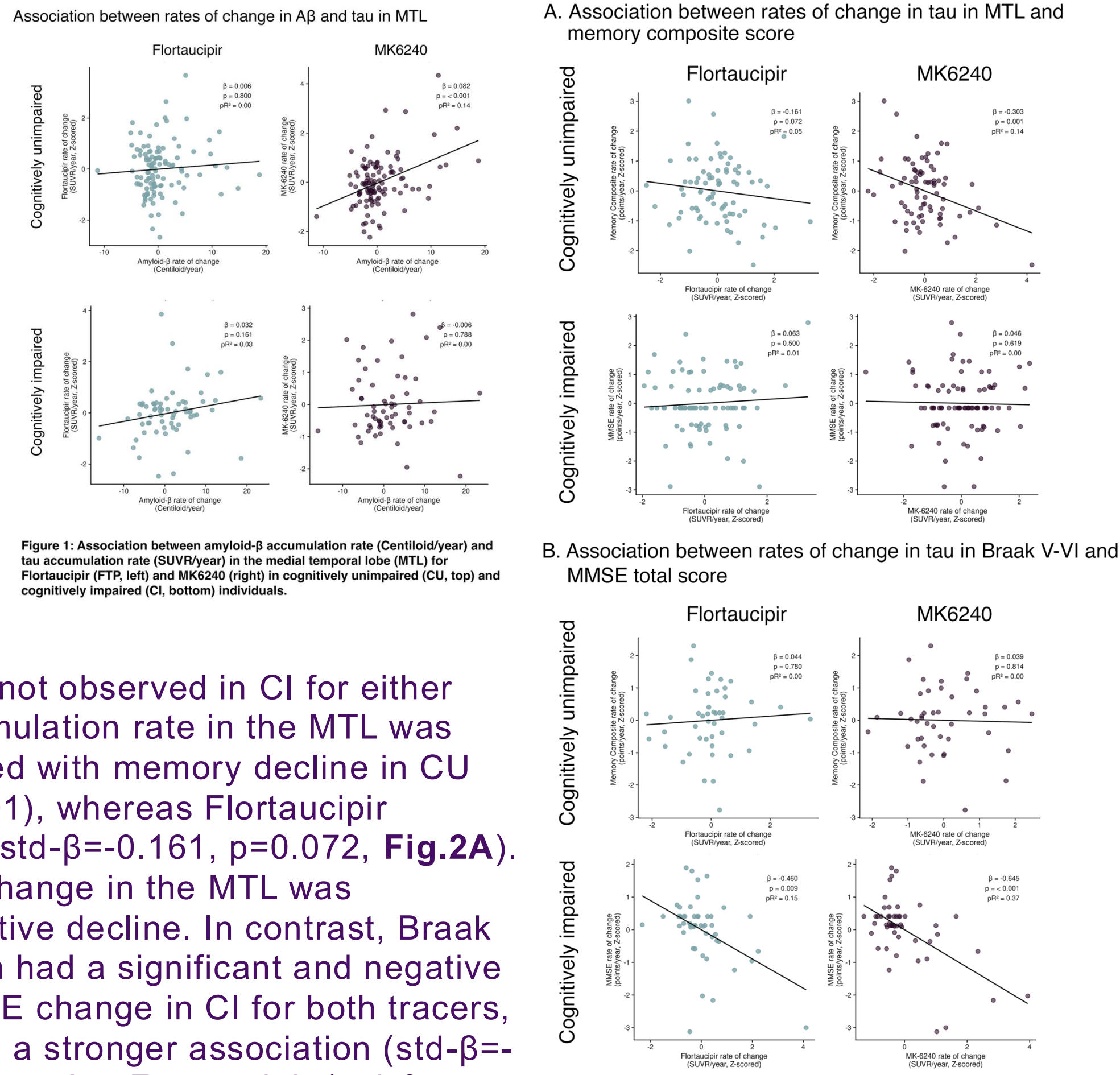
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INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
Tau-PET tracers are used to identify and monitor tau pathology progression in Alzheimer's disease (AD). However, different tau-PET tracers exhibit distinct performance profiles in detecting longitudinal tau changes. Here, we compared longitudinal associations between Flortaucipir and MK6240 and amyloid accumulation and cognitive decline.	We assessed 201 individuals [119 cognitively unimpaired (CU; 17.6% Aβ+), 67 cognitively impaired (CI; 64.2% Aβ+)] with head-to-head Flortaucipir and MK6240 (18-month follow-up). Individuals receiving anti-amyloid therapies between time points were excluded. SUVRs were calculated using inferior cerebellar gray matter as reference. Tau was quantified in the medial temporal lobe (MTL) and Braak V-VI region. Amyloid was quantified using the standard Centiloid mask. Cognition was measured with Mini-Mental State Exam (MMSE) and a memory composite score. Rates of change were calculated as follow-up minus baseline divided by time in years.	In CU, MK6240 detected a significant positive association between amyloid accumulation rate and tau accumulation rate in the MTL (std-β=0.082, p<0.001), while Flortaucipir did not (std-β=0.006, p=0.800, Fig.1). This association was not observed in CI for either tracer. MK6240 accumulation rate in the MTL was significantly associated with memory decline in CU (std-β=-0.303, p=0.001), whereas Flortaucipir showed only a trend (std-β=-0.161, p=0.072, Fig.2A). In CI, neither tracer change in the MTL was associated with cognitive decline. In contrast, Braak V-VI tau accumulation had a significant and negative association with MMSE change in CI for both tracers, with MK6240 showing a stronger association (std-β=-0.645, p<0.001) compared to Flortaucipir (std-β=-0.460, p=0.009, Fig.2B). No significant associations between tau and cognition changes were observed in CU for the Braak V-VI region.	Our preliminary results indicate that MK6240 showed greater sensitivity than Flortaucipir in detecting early tau associations with amyloid and memory decline in MTL in CU. In CI, both tracers captured associations between neocortical tau accumulation and global cognitive decline, consistent with the expected progression of tau pathology across the AD spectrum.





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