Assessing decline in visuospatial working memory associated with subjective cognitive impairment using a novel tablet-based measure of hippocampal-dependent learning

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Methodological Issue

Improved methodologies to facilitate identification, screening, and enrollment for clinical drug trials in preclinical AD populations.

Background

Impairment in visuospatial working memory related to hippocampal-dependent binding of stimulus features has been suggested as a potential early marker AD neuropathology. Prior work in this area has shown that subjects with mild cognitive impairment may not differ from healthy controls in basic working memory tasks, but tasks that require encoding and maintenance of combined object features, such as identity and location, demonstrate increased sensitivity. The specificity of these deficits indicates a relationship between task performance and reduced integrity of the hippocampal, perirhinal and entorhinal cortices which are affected early in AD pathology, and suggests that a sensitive measure of

visuospatial working memory may serve as an ideal screening tool in preclinical AD. We describe results of a recent study utilizing a novel tablet-based visuospatial working memory (VSWM) screening measure.

Methods

Participants included 168 healthy young adults (YA, <55 years), 275 healthy older adults (OA, ≥55 years), and 60 individuals with subjective cognitive decline (SCD). Participants with SCD were categorized as such based on total scores of ≥ 4 on the Cognitive Function Instrument (CFI). Participants completed the VSWM task along with additional measures of cognition and function at two study visits approximately 1 week apart. Group differences in VSWM total score were assessed, as were differences in Sequential and Random sub-scores. P-values for post-hoc pairwise comparisons were corrected using the Bonferroni procedure. Intraclass correlation coefficients (ICC, two-way random effects model for absolute agreement) were computed to assess test-retest reliability.

Results

Statistically significant differences were demonstrated among the three groups for the VSWM total score as well as the Sequential and Random subscores ($p<.001$ for all). Bonferroni post hoc tests showed significant differences between the YA group, the OA group and the SCD group, with the OA group performing significantly worse than the YA group and the SCD group performing significantly worse than the OA group on three measures ($p\leq0.001$ for all comparisons). The SCD group performed significantly worse than the OA group on standard objective cognitive tests ($p<.001$ for all), suggesting concordance between subjective and objective cognitive decline. On the MoCA, the SCD group performed 0.92 SDs (2.67 points) lower than the OA group. On the TMT-B, the SCD group took an average of 37.62 seconds (0.69 SDs) longer than the OA group to complete the task. Test-retest

reliability of the VSWM test was strong. ICCs for VSWM total scores were .82 for YAs, .78 for OAs and .81 for participants with SCD.

Conclusions

A brief assessment of visuospatial working memory is sensitive to differences between healthy older adults with and without subjective cognitive decline, suggesting the instrument may be sensitive to the earliest stages of cognitive impairment. The specificity of observed declines in hippocampal-dependent tasks such as this offer a link to underlying AD pathology not provided by more global cognitive screening instruments.