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

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BACKGROUND

- Clinical drug trials in preclinical AD populations will require novel approaches to participant identification, screening, and enrollment.
- Cognitive screening instruments must be straightforward, sensitive to disease-specific pathology, and allow for the interpretation of findings over time relative to demographically age-matched normative samples.
- Well-designed assessments of visuospatial working memory may serve as fruitful screening measures.
  - Specific impairments in visuospatial working memory related to hippocampal-dependent binding of stimulus features have 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 suggests a potential relationship between task performance and reduced integrity of the hippocampal, perirhinal and entorhinal cortices which are affected early in AD pathology.
- We describe results of a recent study utilizing a **novel tablet-based visuospatial working memory (VSWM) task** to examine differences between healthy older adults with and without subjective cognitive decline (SCD).

METHODS

Participants

- Participants included 175 healthy young adults (YA, <55 years), 320 healthy older adults (hOA, ≥55 years), and 70 individuals with subjective cognitive decline (SCD). Participants with SCD were categorized as such based on total scores of ≥ 4 on the Mail-In Function Cognitive Screening Instrument (MCSFI). Participant characteristics are displayed in Figure 1.
- Participants completed the VSWM task (Figure 2) along additional assessments of cognition and function at two study visits approximately 1 week apart.

Figure 1. Participant Characteristics

		YA	hOA	SCD
SEX	Female (count)	93	169	48
	Male (count)	82	151	22
AGE (years)	Mean	39.55	68.57	71.90
	SD	10.41	8.36	9.39
EDUCATION (years)	Mean	13.89	14.88	14.66
	SD	2.15	2.70	2.43

Analysis

- Group differences in VSWM total score were assessed, as were differences in Sequential and Random sub-scores; group differences in performance on standard cognitive measures were also assessed.
- 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: *Standard Cognitive Measures*

- The SCD group performed significantly worse than the OA group on standard objective cognitive tests (p<.001 for all), indicating concordance between subjective and objective cognitive decline.
- On the MoCA (Fig. 3A), the SCD group performed 0.92 SDs (2.67 points) lower than the hOA group.
- On the TMT-B (Fig. 3B), the SCD group took an average of 37.62 seconds (0.69 SDs) longer than the OA group to complete the task.

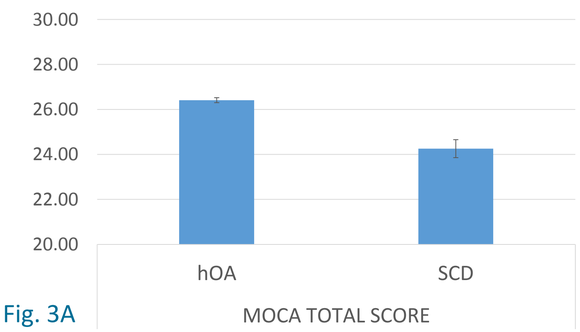

Fig. 3A

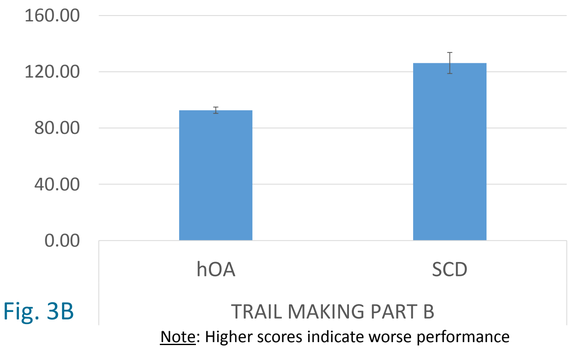

Fig. 3B

Note: Higher scores indicate worse performance

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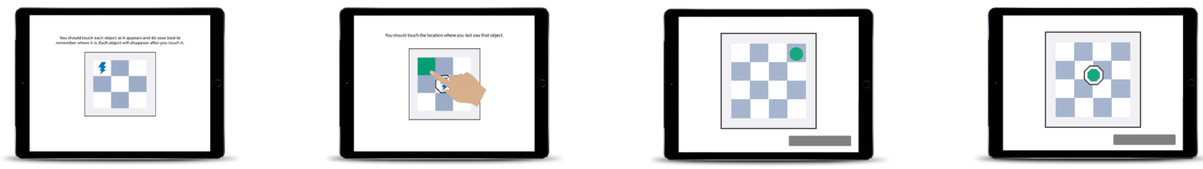
Figure 2. Visuospatial working memory task

Sequence length and grid size increase incrementally



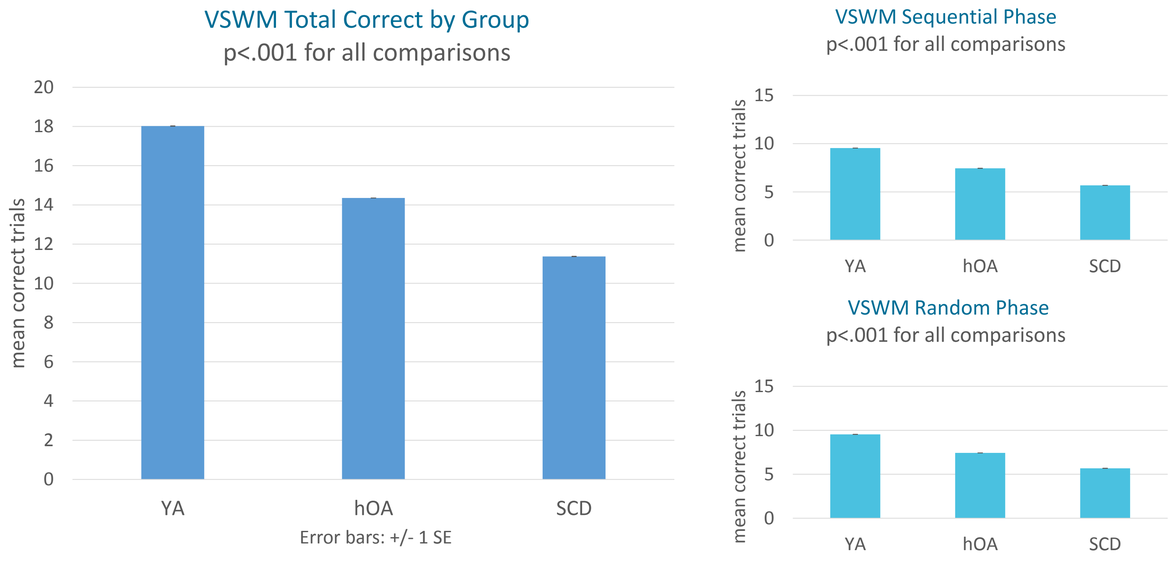
- Participants encoded object-location pairs by tapping items as they appeared in sequence on a grid. Next, a central probe appeared and participants tapped the location where the object first appeared.
- A sequence was considered correct only when each item in the sequence was located correctly. Sequence length and grid size increased throughout the task.
  - In the Sequential portion of the task, memoranda were probed in the order or encoding.
  - In the Random portion of the task, memoranda were probed in random order.
  - The VSWM total score was calculated as the sum of the total sequences correct in the Sequential and Random portions of the task.

RESULTS

VSWM Group Differences

- 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, Figure 4).
- Bonferroni post hoc tests showed a 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≤0.001 for all comparisons).

Figure 4. VSWM performance in YA, hOA and SCD



VSWM Test-Retest Reliability

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.

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