Monthly at-home computerized cognitive testing to detect diminished practice effects in preclinical Alzheimer’s disease

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Objectives

To investigate A) whether monthly assessments of a computerized cognitive composite (C3) could aid in the detection of differences in practice effects (PE) in clinically unimpaired (CU) older adults, and whether diminished PE would be associated with B) AD neuroimaging biomarkers and C) cognitive decline observed on standard annual in-clinic testing.

Methods

Participants and procedures

N=114 CU individuals (age 77.1±4.9, 61% female, MMSE 29±1.3) from the Harvard Aging Brain Study (HABS) completed the self-administered C3 monthly at-home on an iPad for up to one year (11.7±2.8 months follow-up).

At baseline, participants had undergone PIB-PET imaging (1.25±1.05 years within at-home baseline) and Flortaucipir PET imaging (n=109, 0.56±0.4 years within at-home baseline) and in-clinic Preclinical Alzheimer’s Cognitive Composite - 5 (PACC5) testing.

A subsample (n=72, age 78.1±5.2, 59% female, MMSE 29±1.3) also had one year follow-up in-clinic PACC5 testing available.

Computerized Cognitive Composite (C3)

C3 includes the Face Name Associative Memory Exam (FNAME), the Behavioral Pattern Separation Task-Object version (BPSO), and the Cogstate Brief Battery including the One Card Learning task (OCL).

The FNAME, BPSO and OCL accuracy z-scores are combined into a C3 z-score.

Statistical analyses

Linear mixed models (LMM) to investigate C3 performance over time (months) adjusting for age, sex, and years of education, and to extract individual covariate-adjusted C3 slopes over the first 3 months.

Correlations to investigate associations between 3-month C3 slopes (covariate-adjusted) and 1) global amyloid burden (DVR); (2) tau deposition in the entorhinal cortex and inferior-temporal lobe (SUVr, volume-corrected); and 3) change on the PACC5 over one year.

Receiver Operating Curve (ROC) analyses to examine how accurately C3 performance over time (months) adjusting for age, sex, and years of education, and to extract individual covariate-adjusted C3 slopes over the first 3 months could provide a valuable marker to identify individuals who will show more than 0.10 SD annual decline on the PACC5.

TABLE 1. STANDARDIZED TIME ESTIMATES OBTAINED FROM LMM

<table>
<thead>
<tr>
<th></th>
<th>Time change over 12 months</th>
<th>Monthly change over 1st 3 months</th>
<th>P-Value</th>
<th>Time change over 1st 3 months</th>
<th>Monthly change over 1st 3 months</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3</td>
<td>0.226</td>
<td>0.207 – 0.245</td>
<td>&lt;.001</td>
<td>0.665</td>
<td>0.566 – 0.763</td>
<td>&lt;.001</td>
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<tr>
<td>BPSO</td>
<td>0.073</td>
<td>0.061 – 0.085</td>
<td>&lt;.001</td>
<td>0.210</td>
<td>0.148 – 0.271</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>FNAME</td>
<td>0.098</td>
<td>0.088 – 0.108</td>
<td>&lt;.001</td>
<td>0.378</td>
<td>0.328 – 0.429</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>OCL</td>
<td>0.051</td>
<td>0.041 – 0.060</td>
<td>&lt;.001</td>
<td>0.074</td>
<td>0.021 – 0.127</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*Time estimates obtained from LMM adjusting for age, sex and years of education. All scores are z-transformed to facilitate comparisons across measures and follow-up durations. C3 z-score combining BPSO + FNAME + OCL scores.

Conclusion

A. Overall, CU adults show practice effects (PE) on monthly repeated computerized testing, and PE are strongest over initial repeated exposures (i.e., over the first 3 months).

B. However, diminished PE over 3 months are associated with greater AD biomarker burden and cognitive decline over one year.

C. Characterizing PE on the C3 over 3 months could provide a valuable marker to identify individuals who will show more than 0.10 SD annual decline on the PACC5.

Our findings imply that remote computerized testing using monthly retest paradigms can provide rapid detection of diminished PE indicative of future cognitive decline in preclinical AD. This could accelerate clinical trial recruitment and screening as well as the detection of treatment effects.

References:

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