

Summary Abstract:

The explosion of digital technology in the past decade has led to unprecedented possibilities towards improving cognitive assessment and understanding brain health. Digital technology encompasses using a multitude of devices, such as laptops, smartphones, etc, to collect health-related data. The settings can be varied to include in-clinic, remote/virtual, or a combination of hybrid models for data collection. Data can be collected at a single time point or over a continued period of time. Furthermore, the unique combination of devices used, settings, and methods of collecting digital data can become even more exclusive against the backdrop of the 'purpose' for conducting the digital study. This symposium, consisting of four abstracts, brings together the unique combination of digital studies with exclusive devices, methodologies, settings, and purposes. The topics range from how smartphone-based assessments can be applied to understand the interaction between day-to-day variability in sleep and cognition, to the use of computerized testing to investigate the associations between cognitive performance and markers of brain pathology (e.g. amyloid and tau status), to understanding cognition from an open-source smartphone application to passively and continuously capture sensor data including global positioning system trajectories, to the development and validation of an online simulated money management credit card task, and to determining the effects of cognitive rehabilitation via digital technology on cognition, neuropsychiatric symptoms, and memory strategies.

Keyword 1: brain function

Keyword 2: technology

Keyword 3: teleneuropsychology

1 What Can we Learn from High Frequency Smartphone-Based Cognitive Assessments?

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Objective: Smartphone-based cognitive assessments can provide unique information about cognition that is difficult or impossible with traditional cognitive assessments. Using high-frequency measurement "burst" designs, we have shown that older adults are capable and willing to participate in smartphone-based research, that this method dramatically improves between-subject reliability compared to traditional methods and demonstrates extraordinary test-retest reliabilities, and that high-frequency measurement can reveal time of day effects that are increased in those with elevated Alzheimer's disease biomarkers. In this symposium session, we will provide an overview of our current work in older adults at risk for AD and highlight new analyses on the interaction between day to day variability in sleep and cognition. We will also cover our approach for measuring smartphone latencies, a critical aspect of bring-your-own-device (BYOD) studies.

Participants and Methods: The Ambulatory Research in Cognition (ARC) smartphone application for iOS and Android administers custom-designed tests of associate memory, processing speed, and spatial working memory. ARC uses a measurement burst design in which very brief (typically 60s or less) tests are completed at random times several times per day for up to one week. Measurement burst designs rely on principles from ecological momentary assessment, and can be described with a simple formula: 1. Test often and everywhere, 2. Keep assessments brief, and 3. Combine the data across sessions to increase reliability. At the Knight Alzheimer's Disease Research Center at Washington University in St. Louis, we have enrolled over 400 participants (ages 60-99 years) at risk for AD in ARC studies. These participants are comprehensively assessed with traditional cognitive tests, clinical examinations, neuroimaging, and fluid biomarkers. ARC also assesses sleep with the Pittsburgh Sleep Quality Index that captures essential sleep parameters, which are assessed daily during each 7-day measurement burst. Analyses of sleep and cognition focused on parameters including total sleep time, number of awakenings, sleep quality ratings, and an extremes analysis comparing cognition after nights with more sleep and after nights with less sleep.

Results: Overall, participants reporting less total sleep time and more awakenings had lower memory and processing speed scores. This

remained significant after modeling covariates including age, self-reported gender, education, and APOE e4 status. Compared to nights with the most sleep, memory was worse after the nights with the poorest sleep.

Conclusions: When considering AD biomarkers in these analyses, participants with elevated AD biomarkers, including neurofilament light chain (NfL) and phosphorylated-tau181 (p-tau181), demonstrated more impacts of poor sleep on cognition, such that the nights with the least sleep tended to impact cognition more than in those with normal biomarker levels, suggesting an important role for sleep in maintaining cognition in preclinical and early symptomatic AD. Interestingly, self-reported sleep quality was not associated with ARC cognitive tests, consistent with studies emphasizing the need for more quantitative assessments of sleep quality. In addition to these sleep data, we will review publications using the ARC platform, including a recently accepted manuscript in JINS (Nicosia et al., 2022).

Categories: Teleneuropsychology/ Technology

Keyword 1: sleep

Keyword 2: brain function

Keyword 3: cognitive functioning

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2 Computerized Cognitive Practice Effects in Relation to Amyloid and Tau in Preclinical Alzheimer's Disease: Results from a Multi-Site Cohort

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Objective: There is a need to identify scalable cognitive paradigms that are sensitive enough to relate to Alzheimer's disease biomarkers (amyloid and tau) in the preclinical stage. Here, we determine whether initial performance and practice effects on the memory-focused Computerized Cognitive Composite (C3) relate

to demographic variables, amyloid status [abnormal (A+), normal (A-)], and regional tau in clinically unimpaired (CU) older adults.

Participants and Methods: We examined pre-randomization data from CU older adults screened for the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) study. We focused on participants who completed the C3 (n=3287), most of whom completed an alternate version of the C3 again approximately 51 days later (n=4141), as well as a subset of preclinical AD participants (i.e., A+ CU) who completed the C3 and tau PET imaging with [18]F-flortaucipir (initial C3: n=354; repeat C3: n=343). C3 initial performance and practice effects were examined in relation to amyloid status (A+, A-) and continuous regional tau burden.

Results: Initial C3 performance was associated with amyloid status [B(SE) = -0.075 (0.021), $p < 0.001$] across all participants, as well as tau burden in the medial temporal lobe (MTL) [B (SE) = -0.728 (0.220), $p = 0.001$], inferior temporal (IT) cortex [B (SE) = -0.782 (0.264), $p = 0.003$], and inferior parietal (IP) cortex [B (SE) = -0.721 (0.281), $p = 0.011$] amongst preclinical AD individuals. Short-term practice effects were also associated with reduced tau burden in MTL [B (SE) = -0.471 (0.202), $p = 0.020$], IT [B (SE) = -0.640 (0.240), $p = 0.008$], and IP [B (SE) = -0.584 (0.255), $p = 0.023$] amongst preclinical AD participants, but were not associated with amyloid status [B (SE) = -0.018 (0.020), $p = 0.348$]. Critically, these effects with tau were only detected when baseline performance was accounted for presumably due to opposing influence from both practice effects and regression to the mean effects.

Conclusions: This is the first study to show that performance on a brief cognitive battery administered in a multisite context is associated with both amyloid and tau among CU older adults. These findings suggest that computerized assessments may be a cost-effective and scalable approach for early detection efforts. Further, diminished practice effects on memory-based measures are associated with elevated tau burden in preclinical AD, suggesting that high-frequency cognitive testing collected over a short follow-up period may provide additional insights regarding early disease processes than single assessments.

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