Power analysis methods accounting for high intra-individual variability in measured cognition

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What is the Methodological Issue Being Addressed? Power analyses, conducted to determine the required sample size of a trial, traditionally account for between-person variability and within-person changes over time, and generally assume relative intra-individual stability, homogeneity of variances between groups, and a normally distributed latent variable (i.e., the concept of interest that cannot be directly measured). When these assumptions are untrue, traditional power analyses may underestimate the required sample size, potentially resulting in under-powered trials.

Measures of cognitive function, such as those used in Alzheimer's disease, challenge these assumptions. They have been consistently observed to produce high intra-individual- compared to between-person variability, a pattern that is exacerbated in people with dementia, a population of great interest for clinical trials. Additionally, it is common for cognitive tasks to use task-related time measurements such as response time (e.g., as a proxy for processing speed), which tend to produce skewed rather than normal distributions.

Introduction A simulation-based power analysis was conducted that accounted for both between-person and intra-individual variability in measured cognition, and a potentially skewed outcome distribution.

Methods A Monte Carlo simulation study with 500 replications per condition was conducted based on published parameters from ecological momentary assessments of cognition collected in older adults with and without mild cognitive impairment (Cerino, Katz, et al., 2021, doi: 10.3389/fdgth.2021.758031). The study investigated the power resulting from varying sample sizes for the evaluation of group differences, as well as psychometric properties including test-retest reliability and responsiveness (i.e., ability to detect change; separate simulations were conducted for each of these), and also compared the effect of normal vs skewed outcome distributions. The study assumed cognitive assessments would occur at clinic visits, with the first two visits occurring one week apart and subsequent visits occurring six months apart. An additional condition assessed whether inclusion of a second administration of the cognitive task, within the same clinic visit, would increase the resulting power. A range of values were chosen for the population group differences, reliability, change from baseline, and any relationships between variables.

The power analysis was conducted for the Virtual Reality Functional Capacity Assessment Tool – Short List (VRFCAT-Slx), but the same methods are applicable to other measures of cognitive

performance.

Results Compared to a traditional power analysis, accounting for intra-individual variability in cognition and a potentially skewed outcome distribution across most conditions resulted in a larger minimum sample size required to achieve power ≥0.80. Additionally, including two assessments per clinic visit decreased the minimum required sample size compared to one assessment. For one representative condition, the sample size was 150 (normal distribution) or 200 (skewed) under a traditional power analysis but 300 or greater when accounting for intra-individual variability; including a second assessment decreased this to 150 (normal) or 300 (skewed).

Conclusion These results highlight the importance of accounting for characteristics of the data distribution and any unusual properties of the concept of interest when conducting power analyses. In this example, a traditional power analysis that accounts for only between-person variability and assumes the outcome is normal would underestimate the minimum required sample size.

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Guidelines I have read and understand the Poster Guidelines

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