

Challenges and Strategies for Measuring Biomarkers of Cognitive Change in Older Adults

Nurse scientists have traditionally focused on behavioral interventions to promote health, treat symptoms, and improve health outcomes in older adults. Thought leaders in geriatric research, funding agencies, and the aging population are interested in the effect of behavioral interventions (e.g., exercise, social activity, sleep promotion) on the trajectory of Alzheimer's disease (AD). Molecular and neuroimaging biomarkers, such as structural magnetic resonance imaging (MRI), fluorodeoxyglucose positron tomography, and cerebrospinal fluid tau, have enabled scientists to better predict pathologies underlying AD, formulate diagnostic criteria, and quantify responses to interventions. Molecular and neuroimaging biomarkers are increasingly used in behavioral intervention research. The current editorial shares some of the challenges encountered while using structural MRI biomarkers in a behavioral intervention study on the effect of continuous positive airway pressure (CPAP) on cognitive and everyday function in older adults with mild cognitive impairment and obstructive sleep apnea (Richards et al., 2011). Strategies used by the research team to address and overcome the challenges are also described. Lessons learned by these researchers will hopefully help gerontological researchers with planning for the requisite budget, sampling, and procedural needs during the preproposal phase of their projects.

The purpose of MEMORIES (Mild Cognitive Impairment and Obstructive Sleep Apnea) is to estimate the effect size associated with obstructive sleep apnea on cognitive and everyday function in older adults with mild cognitive impairment. The researchers also aim to explore the validity of specific neuroimaging biomarkers for quantifying the effects of CPAP on the brain. MEMORIES is a 3-year, multisite, longitudinal pilot study. The MRI scanning protocol mirrors standardized methods in the AD Neuroimaging Initiative (ADNI) (Jack et al., 2008).

Challenges associated with structural MRI in the MEMORIES study were differences in MRI scanners among sites, MRI costs that exceeded the budget, and recruitment challenges. The analysis protocol required a 3 Tesla scanner. One of the MEMORIES sites had applied for funding to replace its scanner with a 3 Tesla scanner; however, the funding was not granted, and the older scanner could not be used for the study. Although 3 Tesla scanners were available in practice settings located within 15 to 20 minutes of the study site, the quoted scanning costs were four times the budgeted amount. Fortunately, the researchers were able to contract with an ADNI site at a university medical center approximately 1 hour away. However, the scanning costs averaged \$100 more for each scan than the researchers' budget.

The unplanned MRI site added additional costs to the budget. Staff hours increased for screening at the new site, and mileage reimbursement for project staff increased because of the longer commute. Although most participants chose to drive their personal vehicles to the medical center for MRI scanning, some participants required public transportation, which was another unplanned cost.

Another unanticipated cost was radiologist review of the scans for aneurysms and other potentially life-threatening structural abnormalities. Peer reviewers and the investigators were concerned for the rights of human subjects; therefore, they required that participants who chose to be informed receive the results of their MRI scans. Although the group of coinvestigators included physicians and scientists with neuroimaging expertise, none were radiologists. Therefore, a radiologist was needed to review and write the interpretation of the MRI, and the physician coinvestigators helped with medical follow up.

A third challenge was recruitment of participants for the MRI portion of the study. Early into study recruitment,

several potential participants who qualified and were interested in partaking in the study were unable to participate due to MRI exclusions (e.g., implanted metal) or because they did not want to undergo MRI scanning due to claustrophobia or other concerns. To address recruitment challenges associated with MRI scanning, the consent was revised to make the MRI portion of the study optional. Although this strategy reduced the sample size for the MRI portion of the study by approximately 20%, it allowed researchers to better meet recruitment goals for the primary study aim.

In summary, investigators interested in measuring structural MRI biomarkers should (a) anticipate scanner requirements for data analysis prior to identifying study sites; (b) budget for all potential MRI costs, including costs for staff and participant transportation and medical review of scans; and (c) anticipate the effect of MRI exclusions and claustrophobia on recruiting the required sample.

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