aMCI relative to the other two groups in both fluency conditions, suggesting pupil dilation informs risk beyond information provided by task performance.
Conclusions: In a previous sample of community-dwelling men who were an average of 13 years younger than the present sample, we found significantly greater pupil dilation during a digit span task in aMCI relative to naMCI and CN groups. In the present study, we replicated those findings in an older sample using a different cognitive task. Significantly greater pupil dilation was found in individuals with aMCI on verbal fluency tasks, indicating greater compensatory cognitive effort to maintain performance. Pupillometry provides a promising biomarker that might be used as an inexpensive and noninvasive additional screening tool for risk of AD.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: dementia - Alzheimer's disease
Keyword 2: effort testing
Keyword 3: verbal abilities
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52 Bayesian Logistic Regression Bias Adjustment for Data Observed without a Gold Standard: A Simulation Study of Clinical Alzheimer's Disease

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Objective: Definitive diagnosis of Alzheimer's disease (AD) is often unavailable, so clinical diagnoses with some degree of inaccuracy are often used in research instead. When researchers test methods that may improve clinical accuracy, the error in initial diagnosis can penalize predictions that are more accurate to true diagnoses but differ from clinical diagnoses. To address this challenge, the current study investigated the use of a simple bias adjustment for use in logistic regression that accounts for known inaccuracy in initial diagnoses.
Participants and Methods: A Bayesian logistic regression model was developed to predict unobserved/true diagnostic status given the sensitivity and specificity of an imperfect reference. This model considers cases as a mixture of true (with rate = sensitivity) and false positives (rate = 1 – specificity) while controls are mixtures of true (rate = specificity) and false negatives (rate = 1 – sensitivity). This bias adjustment was tested using Monte Carlo simulations over four conditions that varied the accuracy of clinical diagnoses. Conditions utilized 1000 iterations each generating a random dataset of n = 1000 based on a true logistic model with an intercept and three arbitrary predictors. Coefficients for parameters were randomly selected in each iteration and used to produce a set of two diagnoses: true diagnoses and observed diagnoses with imperfect accuracy. Sensitivity and specificity of the simulated clinical diagnosis varied with each of the four conditions (C): C1 = (0.77, 0.60), C2 = (0.87, 0.44), C3 = (0.71, 0.71), and C4 = (0.83, 0.55), which are derived from published values for clinical AD diagnoses against autopsy-confirmed pathology. Unadjusted and bias-adjusted logistic regressions were then fit to the simulated data to determine the models' accuracy in estimating regression parameters and prediction of true diagnosis.
Results: Under all conditions, the bias-adjusted logistic regression model outperformed its unadjusted counterpart. Root mean square error (the variability of estimated coefficients around their true parameter values) ranged from 0.23 to 0.79 for the unadjusted model versus 0.24 to 0.29 for the bias-adjusted model. The empirical coverage rate (the proportion of 95% credible intervals that include their true parameter) ranged from 0.00 to 0.47 for the unadjusted model versus 0.95 to 0.96 for the bias-adjusted model. Finally, the bias-adjusted model produced the best overall diagnostic accuracy with correct classification of true diagnostic values about 78% of the time versus 62-72% without adjustment.
Conclusions: Results of this simulation study, which used published AD sensitivity and specificity statistics, provide evidence that bias-adjustments to logistic regression models are needed when research involves diagnoses from an imperfect standard. Results showed that unadjusted methods rarely identified true effects with credible intervals for coefficients including the true value anywhere from never to less than half of the time. Additional simulations are

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needed to examine the bias-adjusted model's performance under additional conditions. Future research is needed to extend the bias adjustment to multinomial logistic regressions and to scenarios where the rate of misdiagnosis is unknown. Such methods may be valuable for improving detection of other neurological disorders with greater diagnostic error as well.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: psychometrics
Keyword 2: test theory
Keyword 3: target detection
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53 Case Study Comparison of Logopenic and Semantic PPA Variants within the Medically Complex Veteran Population

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Objective: To explore the utility of neuropsychological testing for patients with Primary Progressive Aphasia and compare testing data for a Logopenic and Semantic PPA variants within the medically complex Veteran population.
Participants and Methods: Both participants were referred by their psychiatrist due to memory concerns. The case studies testing data will be compared to look at the differences on testing between different PPA presentations within the Veteran population. Patient A is a 77 year old, right handed, African American, divorced man with approximately 14 years of formal education. Patient B is a 76 year old, right handed, Caucasian, widowed man with approximately 16 years of formal education.
Results: Patient A displayed problems with single-word retrieval, repetition of nonsense words and sentences, comprehension, reading, spelling, and naming. He also displayed impairments in aspects of working memory, along with learning and memory. His cognitive profile raises concern for a logopenic variant of primary progressive aphasia, which often has Alzheimer's disease pathology. Patient B displayed empty speech, impairments in fluency and reduced semantic knowledge that raises concern for a semantic variant of primary progressive aphasia. However, aspects of his presentation are not consistent with this diagnosis, specifically intact confrontation visual naming. Patient has a history of significant alcohol abuse, although he has mostly remained sober since moving to Texas. This evaluation cannot rule out the contribution of sustained alcohol use on his cognitive functioning; however, this is likely not the primary etiology given his significant language issues.
Conclusions: Patients with medically complex histories and unclear timelines of symptom progressive make it difficult for diagnostic clarity. Diagnoses can be additionally difficult to determine at times when the clinical presentation is not as clearly defined in textbooks. This case study comparison displays the importance of integrating all data to determine the proper diagnosis to optimize patient care and provide recommendations tailored to that individual.

Categories: Dementia (Non-AD)
Keyword 1: aphasia
Keyword 2: dementia - other cortical
Keyword 3: aging disorders
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54 Neuropsychiatric Symptoms in Mild Cognitive Impairment and Dementia with Lewy Bodies

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Objective: Neuropsychiatric symptoms (NPS) can be observed in mild cognitive impairment (MCI) and dementia. Hallucinations are a core clinical symptom of Dementia with Lewy Bodies (DLB). In this study, we investigated NPS in healthy control and MCI groups who would later

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