0.0495). Specifically, higher polygenic risk was associated with lower Aβ 42/40 ratio, suggesting greater Aβ burden in the brain, among those with a history of TBI (*pr* = -0.33, *P* = 0.024) compared to individuals without a history of TBI (*pr* = 0.17, *P* = 0.308). This relationship trended towards being stronger as a function of increasing TBI severity ($F(2, 77) = 3.01$, $P = 0.055$).
Conclusions: These results show that, in the context of TBI, higher genetic risk for AD is associated with greater AD-related pathology, particularly with more severe injuries. TBI and polygenic risk may implicate similar biological pathways, notably amyloid precursor protein processing, to increase Aβ burden in the brain and likelihood of progression to AD in future years. These findings could inform early intervention techniques to delay or preclude conversion to AD.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: dementia - Alzheimer's disease
Keyword 2: traumatic brain injury
Keyword 3: genetics
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29 Smoking as a Risk Factor: Altered Brain Activity in Areas Associated with Preclinical Alzheimer's Disease

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Objective: Those at genetic risk for Alzheimer's Disease (AD) because of the ApoE ε4 allele show differences in activation during olfactory information processing and memory in areas such as MTL structures, entorhinal cortex, posterior cingulate, precuneus, and inferior parietal lobule, suggesting preclinical AD neuropathology and olfactory impairment as a biomarker for predicting later AD onset (Murphy, 2019). The effects of smoking on AD have varied, with early studies suggesting either no effect or protective effects, and recent studies suggesting smoking as a risk factor for AD but with the need for further investigation in preclinical stages. Therefore, this study focused on olfaction and smoking as risk factors for preclinical AD neuropathology by studying differences in fMRI BOLD signal changes in smokers and nonsmokers during olfactory tasks.
Participants and Methods: Archival data from 25 non-demented older adults recruited from the UCSD Alzheimer's Disease Research Center who completed an Assessment Scale-Cognitive Subscale (ADAS-Cog) and functional MRI scans at 3T, acquired during performance of an odor identification task. Odor Identification (OI) measured correct (hits) or incorrect (misses) identification of odors presented by an olfactometer to deliver the odor stimuli in short, controlled durations during fMRI scanning.
Results: fMRI data were preprocessed using fMRIprep, smoothed at 4mm, scaled, and first level analyses were conducted using 3dDeconvolve in AFNI with time points corresponding to hits and misses as regressors. Differences between smokers and nonsmokers revealed smokers show a larger difference in BOLD signal change from hits minus misses at five significant clusters ($p = 0.01$ with the minimum cluster size [voxels] at 42). Peak areas of significant clusters included the right precuneus, right calcarine gyrus, left inferior parietal lobule, left superior parietal lobule, and left middle occipital gyrus. Analyses suggested a greater difference in activity between hits and misses in smokers compared to nonsmokers, with more activity during hits.
Conclusions: Differences in activation between smokers and nonsmokers during an olfactory identification task, with greater activity in smokers during hits, suggests greater effort to correctly identify an odor. These findings of hyperactivation in areas (such as the precuneus and inferior parietal lobule) are similar to findings of hyperactivation during odor memory observed in studies of ε4 carriers during preclinical stages. Results provide further insight into smoking as a risk factor for AD. Moreover, results suggest the risk of smoking could potentially be reflected in altered activity in olfactory information processing networks in preclinical stages of AD. The study highlights the need for research to further understand the role smoking plays in the development of AD and the use of olfaction as a biomarker to aid in disease detection, prevention, and stage-associated treatments.

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30 Item response theory and differential item functioning of the AD8: The High School & Beyond Study

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Objective: The AD8 is a validated screening instrument for functional changes that may be caused by cognitive decline and dementia. It is frequently used in clinics and research studies because it is short and easy to administer, with a cut off score of 2 out of 8 items recommended to maximize sensitivity and specificity. This cutoff assumes that all 8 items provide equivalent "information" about everyday functioning. In this study, we used item response theory (IRT) to test this assumption. To determine the relevance of this measure of everyday functioning in men and women, and across race, ethnicity, and education, we conducted differential item functioning (DIF) analysis to test for item bias.
Participants and Methods: Data came from the 2021 follow up of the High School & Beyond cohort (N=8,690; mean age 57.5 ± 1.2; 55% women), a nationally representative, longitudinal study of Americans who were first surveyed in 1980 when they were in the 10th or 12th grade. Participants were asked AD8 questions about their own functioning via phone or internet survey. First, we estimated a one-parameter (i.e., differing difficulty, equal discrimination across items) and two-parameter IRT model (i.e., differing difficulty and differing discrimination across items). We compared model fit using a likelihood-ratio test. Second, we tested for uniform and non-uniform DIF on AD8 items by sex, race and ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic), education level (high school or less, some college, BA degree or more), and survey mode (phone or internet). We examined DIF salience by comparing the difference between original and DIF-adjusted AD8 scores to the standard error of measurement of the original score.
Results: The two-parameter IRT model fit the data significantly better than the one-parameter model, indicating that some items were more strongly related to underlying everyday functional ability than others. For example, the "problems with judgment" item had higher discrimination (more information) than the "less interest in hobbies/activities" item. There were significant differences in item endorsement by race/ethnicity, education, and survey mode. We found significant uniform and non-uniform DIF on several items across each of these groups. For example, for a given level of functional decline (theta) White participants were more likely to endorse "Daily problems with thinking/memory" than Black and Hispanic participants. The DIF was salient (i.e., caused AD8 scores to change by greater than the standard error of measurement for a large portion of respondents) for those with a college degree and phone respondents.
Conclusions: In a population representative sample of Americans ~age 57, the items on the AD8 contributed differing levels of discrimination along the range of everyday functioning that is impacted by later life cognitive impairment. This suggests that a simple cut-off or summed score may not be appropriate since some items yield more information about the underlying construct than others. Furthermore, we observed significant and salient DIF on several items by education and survey mode, AD8 scores should not be compared across education groups and assessment modes without adjustment for this measurement bias.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: cross-cultural issues
Keyword 2: mild cognitive impairment
Keyword 3: psychometrics
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