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Objective: Higher educational attainment is associated with reduced risk for Alzheimer's disease (AD) dementia, and its protective effect may act through alterations in cerebral blood flow (CBF) that allow for better coping with accumulating neuropathology. Additionally, there are sex differences in both the risk of developing AD as well as the potential protective effects of education. We therefore sought to investigate whether education moderates the association of hippocampal CBF and memory in cognitively unimpaired older adults, and to examine if these interactions were moderated by sex.
Participants and Methods: Cognitively unimpaired older adults from the Alzheimer's Disease Neuroimaging Initiative (ADNI; 51 men, 50 women) underwent neuropsychological evaluation and arterial spin labeling MRI, which was used to quantify bilateral hippocampal CBF. Sex was defined as sex at birth. Multiple linear regressions assessed (1) the independent associations among education, CBF, and memory performance separately in men and women and (2) the three-way interactions among CBF, sex, and education, followed by sex-stratified analyses. Three outcome measures were examined: Logical Memory Story A immediate and delayed recall, and Rey Auditory Verbal Learning Test (RAVLT) intrusions. All models adjusted for age and APOE epsilon-4 allele frequency, and all models with CBF additionally adjusted for cerebral metabolism (baseline FDG-PET composite) and pulse pressure.
Results: CBF was not associated with education or memory in either women or men. There was a positive association between education and delayed memory in women (β=0.14, t=2.64, p=0.008) as well as trending, positive associations between education and immediate memory in women (β=0.09, t=1.79, p=0.074) and education and delayed memory in men (β=0.09, t=1.94, p=0.054). Three-way interactions among sex, CBF, and education were significant on immediate recall (β=2.55, t=2.53, p=0.013), delayed recall (β=2.56, t=2.44, p=0.017), and RAVLT intrusions (β=-2.28, t=-2.27, p=0.026). In women, there were interactions between education and hippocampal CBF on both immediate (β=2.49, t=2.90, p=0.006) and delayed recall (β=2.30, t=2.78, p=0.009), such that as education increased, the strength of the association between CBF and immediate memory increased. There was also an interaction between education and hippocampal CBF on RAVLT intrusions in women (β=-2.42, t=-3.05, p=0.004), such that as education increased, the strength of the association between CBF and number of intrusions decreased; there was a main effect where in women with lower education, as CBF increased, the number of intrusions increased (β=0.76, t=2.59, p=0.032); in women with higher education, there was no association between CBF and intrusions. In men, none of these two-way interactions were significant.
Conclusions: These results suggest that, in cognitively unimpaired older women, the relationship between hippocampal CBF and memory is moderated by education level, even when adjusting for several other factors. Specifically, higher education may serve as a protective factor in the hippocampal CBF-memory relationship, and this relationship was sex-dependent, occurring in women only. Further research is needed to examine these relationships longitudinally across the clinical continuum of AD. Additionally, this work needs to be conducted in more diverse samples to allow for analyses investigating the impact of education on the intersection of race/ethnicity and sex/gender.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: cerebral blood flow
Keyword 2: cognitive reserve
Keyword 3: dementia - Alzheimer's disease
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18 Illustrating Alzheimer's: The Role of Visuospatial Abilities in Figure Copying

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Objective: Due to the pathology of Alzheimer's disease (AD), it is not uncommon for patients to struggle with cognitive tasks involving figure copying. However, figure copying requires involvement from multiple other domains, including visuospatial and frontal-executive

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abilities. Less clear is whether figure copying performance, as measured by the Rey-Osterrieth Complex Figure (ROCF), is more affected by visuospatial or frontal-executive compromise in patients with AD. This study aims to discover whether performance on the ROCF varies more with executive or visuospatial abilities in patients with AD.
Participants and Methods: A total of 156 patients (79 women, M age = 77.82, M education = 14.21) diagnosed with Alzheimer's disease (AD) participated in comprehensive neuropsychological assessment as part of outpatient neurology evaluations. In addition to the ROCF Copy trial, participants completed measures of visuospatial function (WAIS-IV Block Design & Picture Completion) and frontal-executive functioning (Trails B, DKEFS Inhibition, WAIS-IV Similarities).
Results: Canonical correlations revealed that ROCF Copy was significantly and positively related to the set of tests measuring visuospatial functioning, $p < .001$, and frontal-executive functioning, $p < .001$. Post-hoc bivariate correlations showed significant positive correlations between ROCF Copy and each visuospatial, $ps < .01$, and each frontal-executive, $ps < .04$, measure. The relationship between ROCF Copy and each visuospatial measure was significantly stronger than the relationship between ROCF Copy and every frontal-executive measure except WAIS-IV Similarities, $ps < .01$. Those with visuospatial impairment (>1.5 SD) performed significantly worse on the ROCF Copy than those without impairment, $p <.01$. This difference persisted even when the effects of frontal-executive measures were controlled, $p < .01$. In contrast, those with frontal-executive impairment did not perform significantly worse on the ROCF Copy than those without frontal-executive impairment, $p < .01$. This did not change when controlling for the effects of visuospatial measures. Finally, the significant difference in ROCF Copy between those with mild cognitive impairment (MCI) and those with dementia ($p < .01$) disappeared when visuospatial measures were controlled, but it remained when frontal-executive measures were covariates, $p < .03$.
Conclusions: These findings suggest the figure copying of those with AD is significantly related to both their visuospatial and frontal-executive functioning, but the relationship with visuospatial functioning is stronger. Impairment in visuospatial, but not frontal-executive, functions, seems to have a negative impact on the figure copying of those with AD, and performance on visuospatial compared to frontal-executive measures better accounts for the weaker ROCF Copy scores among those with dementia relative to MCI. Therefore, the pathological effects of AD on figure copying appear to occur predominantly through visuospatial rather than frontal-executive channels, and interventions for offsetting decline in figure copying may be most effective when targeting visuospatial abilities, such as visual perception and visual construction.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: visuospatial functions
Keyword 2: executive functions
Keyword 3: dementia - Alzheimer's disease
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19 Gray Matter Changes in the Temporal Lobe Moderate the Relationship between CSF Beta-Amyloid and Confrontation Naming Performance

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Objective: Alzheimer's disease (AD) is associated with the accumulation of neuropathological beta-amyloid (Ab) plaques, which is thought to be caused by an imbalance between Ab overproduction and dysfunctional Ab clearance. Both animal and human studies have shown that increased cerebrospinal fluid (CSF) levels of Ab peptides, especially Ab-38 and Ab-40 due to their high solubility, may be indicators of overall Ab dysregulation in preclinical AD, years before pathological Ab plaques begin to aggregate. This overabundance of Ab and later sequestration onto plaques eventually triggers a cascade of subsequent brain changes that may lead to cognitive decline. Indeed, alterations in gray matter integrity may play a role, as imaging studies have shown specific atrophy patterns in preclinical AD, particularly in language regions of the bilateral temporal lobes, which relate to cognitive performance. Here, we aimed to

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