

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

explore whether temporal lobe cortical volume is implicated in the relationship between increased CSF Ab levels and cognitive decline, as measured by confrontation naming performance -- an age-independent language task often impaired in preclinical AD -- in AD-vulnerable populations.

**Participants and Methods:** We selected 87 non-demented Veterans (Sex: 99% male; Age:  $M=68.2$ ,  $SD=3.7$ ; Education:  $M=15.5$ ,  $SD=2.2$ ) from the Alzheimer's Disease Neuroimaging Initiative-Department of Defense (ADNI-DOD) database based on available Boston Naming Test (BNT) scores, CSF measures of Ab-38 and Ab-40, and structural neuroimaging data. The 30-item BNT assessed confrontation naming performance. CSF Ab concentrations were measured using a 2D-UPLC-tandem mass spectrometry method outlined by ADNI-DOD. T1-weighted images were acquired on a 3T scanner and processed by ADNI to calculate cortical volumes (CVs) for regions of interest (ROIs); the present study focused on three bilateral ROIs in the temporal lobe (fusiform gyrus [FFG], inferior temporal gyrus [ITG], and middle temporal gyrus [MTG]). All CVs were adjusted (CV<sub>adj</sub>) for intracranial volume (ICV) using the covariance formula ( $CV_{adj} = CV - b[ICV - \text{mean}(ICV)]$ ). Linear regression models explored the relationship between CSF Ab peptides and BNT with temporal lobe ROIs as moderators using the PROCESS macro.

**Results:** CV of the bilateral FFG significantly moderated the relationship between BNT performance and both CSF Ab-38 ( $p=.025$ ,  $R^2=.05$ ,  $b=.0008$ ) and Ab-40 ( $p=.016$ ,  $R^2=.06$ ,  $b=.0002$ ) levels. We then explored effects of the left and right FFG separately and found that the relationship between CSF Ab-38 and BNT was significantly moderated by the left FFG ( $p=.032$ ,  $R^2=.05$ ,  $b=.0006$ ) and nominally by the right FFG ( $p=.072$ ,  $R^2=.03$ ,  $b=.0006$ ). The relationship between CSF Ab-40 and BNT was significantly moderated by both the left ( $p=.032$ ,  $R^2=.05$ ,  $b=.0001$ ) and right ( $p=.038$ ,  $R^2=.04$ ,  $b=.0001$ ) FFG. CV of the bilateral ITG and MTG had no effect on any model (all  $p > .10$ ).

**Conclusions:** Increased Ab may trigger alterations in neural gray matter integrity, specifically in the FFG of the temporal lobe, and these changes may in turn be implicated in AD-related cognitive decline, particularly in the language domain. These findings suggest that biomarker models incorporating CSF Ab and CV may aid early identification of disease and risk

for cognitive decline in preclinical AD stages, which could help inform early interventions.

**Categories:** Dementia (Alzheimer's Disease)

**Keyword 1:** dementia - Alzheimer's disease

**Keyword 2:** neuroimaging: structural

**Keyword 3:** language

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## 20 Global and Local Semantic Coherence of Spontaneous Speech in Persons with Alzheimer's Disease and Healthy Controls

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**Objective:** Growing evidence demonstrates that subtle changes in spontaneous speech can be used to distinguish older adults with and without cognitive impairment, including those with Alzheimer's disease (AD). Recent work suggests that quantification of the meaningful connectedness of speech -- termed semantic coherence -- may be sensitive to cognitive dysfunction. The current study compared global coherence (GC; the degree to which individual utterances relate to the overall topic being discussed) and local coherence (LC; the degree to which adjoining utterances relate meaningfully to each other) in persons with AD and healthy controls.

**Participants and Methods:** Speech transcripts from 81 individuals with probable AD ( $M_{age} = 72.7$  years,  $SD = 8.8$ , 70.3% female) and 61 healthy controls (HC) ( $M_{age} = 63.9$  years,  $SD = 8.5$ , 62.2% female) from Dementia Bank were analyzed. All participants completed the Cookie Theft and MMSE as part of that larger project. Machine learning analyses of GC and LC were conducted and models evaluated classification accuracy (i.e., AD vs HC) as well as ROC-AUC. Relationships between coherence indices and MMSE performance were also quantified.

**Results:** Though no significant group differences emerged in LC (Estimate = 0.012,  $p = 0.32$ ), persons with AD differed from healthy controls in GC (Estimate = 0.03,  $p = 0.006$ ) and produced less semantically coherent speech. GC indices predicted AD diagnoses