8.51], p<.001), and Low-All Domains (HR 7.21, 95% CI [3.59, 14.48], p<.001) groups had greater risk of progression to MCI/dementia. The Low-Executive group was also twice as likely to progress to MCI/dementia compared to the All-Average group, but did not statistically differ (HR 2.03, 95% CI [0.88,4.70], p=.096). A similar pattern of results was found for progression to DRS score ≤129, with the Low-Executive (HR 2.82, 95% CI [1.26, 6.29], p=.012), Low-Memory/Language (HR 3.70, 95% CI [1.80, 7.56], p<.001) and Low-All Domains (HR 5.79, 95% CI [2.74, 12.27], p<.001) groups at greater risk of progression to a DRS score ≤129 than the All-Average group. The Low-Visuospatial group was also twice as likely to progress to DRS ≤129 compared to the All-Average group, but did not statistically differ (HR 2.02, 95% CI [0.80, 5.06], p=.135).
**Conclusions:** Our results add to a growing literature documenting heterogeneity in the earliest cognitive and pathological presentations associated with Alzheimer's disease and related disorders. Participants with subtle memory/language, executive, and visuospatial weaknesses all declined at faster rates than the All-Average group, suggesting that there are multiple pathways and/or unique subtle cognitive decline profiles that ultimately lead to a diagnosis of MCI/dementia. These results have important implications for early identification of individuals at risk for MCI/dementia. Given that the same classification approach may not be optimal for everyone, determining profiles of subtle cognitive difficulties in CU individuals and implementing neuropsychological test batteries that assess multiple cognitive domains may be a key step towards an individualized approach to early detection and fewer missed opportunities for early intervention.

**Categories:** Aging
**Keyword 1:** aging disorders
**Keyword 2:** mild cognitive impairment
**Keyword 3:** cognitive functioning
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## 3 Type 2 Diabetes Moderates the Association between Amyloid PET and Attention/Executive Functioning in Older Veterans

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**Objective:** Type 2 diabetes (T2D) is a risk factor for cognitive impairment/dementia and has been shown to modify the impact of Alzheimer's disease (AD) biomarkers on cognition and everyday functioning. Studies examining amyloid-β (Aβ), one of the hallmark AD pathologies, have shown mixed results regarding associations of Aβ biomarkers with cross-sectional cognition as well as T2D, though Aβ is generally associated with future cognitive declines. The purpose of the present study is to examine whether T2D impacts the associations between amyloid positron emission tomography (PET) and cognition in older Veterans.
**Participants and Methods:** The current study included 202 mostly male Vietnam-Era Veterans from the Department of Defense-Alzheimer's Disease Neuroimaging Initiative (DOD ADNI) study (age M=69.38 years, SD=4.37; 40% with self-reported T2D) who completed neuropsychological testing and florbetapir PET imaging. The Aβ PET standardized uptake variable ratio (SUVR) was measured using a previously-validated summary SUVR calculated by dividing the mean uptake across 4 AD-vulnerable cortical regions by whole cerebellar uptake. General linear models examined whether T2D moderated the relationship of Aβ PET with memory, attention/executive functioning, and language composite scores. Models adjusted for age, education, apolipoprotein E ε4 carrier status, vascular risk burden, depressive symptoms, post-traumatic stress disorder (PTSD) symptom severity, and history of traumatic brain injury (TBI).
**Results:** There was no main effect of diabetes on memory, attention/executive functioning, or language performance, and higher Aβ PET SUVR was only associated with worse attention/executive functioning performance (β=-.146, 95% CI [-.261, -.031], p=.013). The Aβ PET x T2D interaction was significant for attention/executive functioning such that higher Aβ PET SUVR was associated with lower

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attention/executive functioning scores, but only in those with T2D (β=-.116, [-.225, -.006], p=.038). This interaction was not significant for language or memory.
**Conclusions:** The results show that Aβ may negatively impact attention/executive functioning, but this effect was only found in Veterans with T2D. Prior work has suggested that T2D may be more associated with tau biomarkers than markers of Aβ, so it is possible that the current results are due to a compounding effect of Aβ pathology plus microvascular and/or tau pathology. Notably, the sample was relatively young, a relatively large proportion had elevated PTSD symptoms and/or a TBI history (which have both been shown to relate to attention/executive function), and the measures that made up the attention/executive composite (Trail Making Test A and B) have been shown to be particularly sensitive – all of which may have contributed to the domain-specific effects. Future research is needed to investigate the role that tau and vascular pathology may play in cognition among individuals with T2D. Longitudinal studies are also needed to better understand the timing and progression of these relationships.

**Categories:** Aging
**Keyword 1:** diabetes
**Keyword 2:** dementia - Alzheimer's disease
**Keyword 3:** attention
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## 4 Traumatic Brain Injury Does Not Alter the Course of Neurocognitive Functioning Later in Life

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**Objective:** History of traumatic brain injury (TBI) is associated with increased risk of dementia, but few studies have evaluated whether TBI history alters the course of neurocognitive decline, and existing literature on this topic is limited to short follow-up and smaller samples. The primary aim of this study was to evaluate whether a history of TBI (TBI+) influences neurocognitive decline later-in-life among older adults with or without cognitive impairment [i.e., normally aging, Mild Cognitive Impairment (MCI), or dementia].
**Participants and Methods:** Participants included individuals from the National Alzheimer's Coordinating Center (NACC) who were at least 50 years old and with 3 to 6 visits (M number of visits = 4.43). Participants with any self-reported history of TBI (n = 1,467) were matched 1:1 to individuals with no reported history of TBI (TBI-) from a sample of approximately 45,000 participants using case-control matching based on age (+/- 2 years), sex, education, race, ethnicity, cognitive diagnosis [cognitively normal (CN), MCI, or all-cause dementia], etiology of cognitive impairment, functional decline (Clinical Dementia Rating Scale, CDR), number of Apolipoprotein E4 (*APOE* ε4) alleles, and number of annual visits (3 to 6). Mixed linear models were used to assess longitudinal neuropsychological test composites (using NACC normative data) of executive functioning/attention/speed (EFAS), language, and memory in TBI+ and TBI- participants. Interactions between TBI and demographics, *APOE* ε4 status, and cognitive diagnosis were also examined.
**Results:** Following matching procedures, TBI+ (n=1467) and TBI- (n=1467) groups were nearly identical in age (TBI+ $M$ = 71.59, $SD$ = 8.49; TBI- $M$ = 71.63, $SD$ = 8.44), education (TBI+ $M$ = 16.12, $SD$ = 2.59; TBI- $M$ = 16.10, $SD$ = 2.52), sex (both 55% male), race (both 90% White), ethnicity (both 98% non-Hispanic), *APOE* ε4 alleles (both 0 = 62%, 1 = 33%, 2 = 5%), baseline cognitive diagnoses (both CN = 60%, MCI = 18%, dementia = 12%), and global CDR (TBI+ $M$ = 0.30, $SD$ = 0.38, TBI- $M$ = 0.30, $SD$ = 0.38). At baseline, groups had similar Z-scores of in EFAS (TBI+ $M_{EFAS}$ = -0.02, $SD$ = 1.21; TBI- $M_{EFAS}$ = -0.04, $SD$ = 1.27), language (TBI+ $M_{Language}$ = -0.48, $SD$ = 0.98; TBI- $M_{Language}$ = -0.55, $SD$ = 1.05), and memory (TBI+ $M_{Memory}$ = -0.45, $SD$ = 1.28; TBI- $M_{Memory}$ = -0.45, $SD$ = 1.28). The course of change in neuropsychological functioning worsened longitudinally, but did not differ between TBI groups (p's > .110). There were no significant interactions between TBI history and age, sex,

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