Conclusions: Our findings from this EMA study suggest that when individuals with T1D experience more time in hypoglycemia at night (compared to their average), they have slower processing speed the following day, while same day hypoglycemia and hyperglycemia does not similarly impact processing speed performance. These results showcase the power of intensive longitudinal designs using ambulatory cognitive assessment to uncover novel determinants of cognitive variation in real world settings that have direct clinical applications for optimizing cognitive performance. Future research with larger samples is needed to replicate these findings.

Categories: Cognitive Neuroscience
Keyword 1: ecological validity
Keyword 2: cognitive functioning
Keyword 3: diabetes
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5 Examining the Cognitive, Vascular, and Lifestyle Profiles of Older Adults with Late-Onset Epilepsy

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Objective: Older adults represent the fastest-growing population of individuals with epilepsy with an incidence that peaks after age 65. Patients with late-onset epilepsy (LOE) have a multitude of risk factors for accelerated cognitive and brain aging, including vascular and metabolic risk factors. Despite this, there are few studies investigating the cognitive profiles of older adults with LOE, a neglected area in aging research. We examine the cognitive profiles of older adults with LOE and determine the contribution of demographic and vascular risk factors to impairment.
Participants and Methods: Participants were part of the Atherosclerosis Risk in Communities Study (ARIC) and the incidence of epilepsy was identified using ARIC hospitalization records and Centers for Medicare and Medicaid Services claims data from 1991 to 2015. Approximately 1.8% of the participants with sufficient Medicare coverage data were classified as having LOE (LOE n=281; Non-LOE n=9808). Vascular, lifestyle, and cognitive data were obtained from the ARIC Neurocognitive Study (ARIC-NCS) which consisted of three visits since 2011. Participants with ARIC-NCS visits completed after the onset of seizures were included in the final sample. Non-LOE participants with normal cognition (Black: n=603 and White: n=2543 participants independently) were used to generate z-scores across tests of language, memory, executive function, and processing speed/attention. Impairment was defined as <1.5 standard deviations below the mean of the normative sample. Stepwise regressions were conducted to examine the contribution of demographic (age, race, sex, education) and vascular risk factors (hypertension, diabetes, hyperlipidemia, obesity, smoking) to cognitive performance.
Results: Average age of first seizure of all LOE participants (n=281) was 76.23 (SD=6.24), 55.9% female, 30.7% Black/African American, and the majority had either a college (28.1%) or high school degree (26%). Fifty-six LOE participants had ARIC-NCS visits after the onset of seizures (average age=79.84, SD=5.17, 57.1% female, 32.1% Black). Approximately 67.9% of the sample had at least one vascular risk factor with 81.5% having hypertension, 37% diabetes, 26.4% hyperlipidemia, 20.4% obesity (BMI>30), and 4.5% current smoker. The most frequently impaired domains were language (naming=29.7%; animal fluency=20%; letter fluency=30%) and memory (prose immediate recall=18.4%; prose delayed recall=44.7%; word delayed recall=19.4%). Higher education was associated with better naming (b=0.801, p=0.040). Female sex (b=-0.799, p=0.017) and lower education levels (b=0.418, p=0.050) were associated with poorer immediate prose recall. Older age was associated with poorer delayed prose recall (b=-0.191, p=0.036). Hypertension was associated with worse digit span backward (b=-0.942, p=0.002).
Conclusions: In older adults with LOE, language and memory were the most commonly impaired cognitive domains, similar to studies in early onset epilepsy. Vascular risk factors were prevalent among LOE and hypertension was associated with worse working memory. Further, important demographic factors (sex, education, and age) were associated with the extent of cognitive impairment. Characterizing cognitive profiles in LOE and determining the contribution

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of demographic and vascular factors to impairment could help to identify patients at risk for future cognitive decline and/or the development of LOE itself, as well as interventions aimed at reducing the risk of further decline.

Categories: Epilepsy/Seizures
Keyword 1: aging disorders
Keyword 2: cognitive functioning
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6 The Moderating Role of Physical Activity on Hippocampal Iron Deposition and Memory Outcomes in Typically Aging Older Adults

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Objective: Quantitative Susceptibility Mapping (QSM) is an MRI-based technique that sensitively measures *in-vivo* iron deposition via relaxation and magnetic susceptibility of brain tissue. Iron is essential for brain homeostasis, including oxidative metabolism, formation and maintenance of neural networks, and myelin synthesis. While increased levels of iron deposition occur during normal aging, high levels may have detrimental effects. Previous work has linked excessive brain iron accumulation to oxidative stress, beta-amyloid and tau toxicity, neurodegeneration, and cognitive dysfunction, particularly memory loss. Physical activity, on the other hand, correlates with higher synaptic integrity and memory performance, even in the presence of neuropathology. To date, it is unknown how physical activity may affect iron deposition-related cognition changes. We examined the moderating role of physical activity on the relationship between QSM hippocampal iron deposition and verbal memory in typically aging adults.
Participants and Methods: 62 cognitively unimpaired older adults from the UCSF Memory and Aging Center (age mean(SD) = 78.34(7.28) years; 56% women; education mean(SD) = 17.94(1.72) years; 85% non-Hispanic White) completed neuropsychological testing and brain MRI during annual research visits, followed by Fitbit™ physical activity monitoring for 30 days. Average total daily steps were aggregated. Participants completed 3T Prisma neuroimaging with QSM, and regional iron deposition levels were quantified. All subjects also underwent diffusion tensor imaging (fractional anisotropy). Verbal memory was assessed via long delay free recall scores from the California Verbal Learning Test II (CVLT-II). Linear regression examined verbal memory as a function of hippocampal QSM (bilateral), physical activity, and their interaction. Models covaried for age, sex, and education. Additional models separately examined left and right hippocampal QSM, as well as subcortical QSM to determine lateralization and specificity of verbal memory effects to hippocampal iron deposition, respectively.
Results: Univariably, higher bilateral hippocampal QSM correlated with worse verbal memory (r= 0.35; p= 0.015). Adjusting for demographics, physical activity moderated the relationship between bilateral hippocampal QSM and verbal memory (β= 0.41, p= 0.011), such that at higher levels of physical activity, the negative relationship between hippocampal QSM and verbal memory was significantly attenuated. Results persisted when adjusting for DTI integrity of the uncinate fasciculus and fornix white matter tracts. Lateralization models were both significant, suggesting that results were not dominantly driven by either left (β= 0.34, p= 0.048), or right (β=0.31, p= 0.035) hippocampal QSM. In contrast, subcortical QSM did not correlate with memory performance (r= 0.13, p > 0.05) or interact with physical activity on verbal memory outcomes (p > 0.05).
Conclusions: Physical activity significantly moderated the negative relationship between hippocampal QSM and verbal memory performance. Higher exercise engagement may buffer the adverse effect of hippocampal iron deposition on memory, potentially through its role in maintenance of myelin and synaptic integrity and/or protecting against other neurotoxic events (e.g., oxidative stress, neuronal cell death). Our results support that physical activity continues to be a modifiable risk factor that may offer a protective role in neurobiological pathways of memory and cognitive decline.

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