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Dietary Inflammatory Index and Memory Function: Population-Based National Sample of Elderly Americans

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Abstract

To examine the association between dietary inflammatory potential and memory and cognitive functioning among a representative sample of the U.S. older adult population. Cross-sectional data from the 2011–2012 and 2013–2014 National Health and Nutrition Examination Survey (NHANES) were utilized to identify an aggregate sample of adults 60–85 years of age (N=1,723). Dietary Inflammatory Index (DII®) scores were calculated using 24-hour dietary recall interviews. Three memory-related assessments were employed, including the Consortium to Establish a

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Conflict of Interest

Dr. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina in order to develop computer and smart phone applications for patient counseling and dietary intervention in clinical settings. Drs. Michael Wirth and Nitin Shivappa are employees of CHI.

Authorship

Author EF prepared part of the initial draft of the manuscript. Author NS assisted in the calculation of the DII. Author PL computed the analyses. Authors EF, NS, JM, JH, MW, and PL helped conceptualize the study and provided feedback on various drafts of the manuscript.

Registry for Alzheimer's disease (CERAD) Word Learning subset, the Animal Fluency test, and the Digit Symbol Substitution Test (DSST). Inverse associations were observed between DII scores and the different memory parameters. Episodic memory (CERAD) ($b_{adjusted}$ = −.39; 95% CI: −.79, .00), semantic-based memory (Animal Fluency Test) ($b_{adjusted}$ = −1.18; 95% CI: −2.17, −.20), and executive function and working-memory (DSST) ($b_{adjusted}$ = −2.80; 95% CI: −5.58, −.02) performances were lowest among those with the highest mean DII score. Though inverse relationships were observed between DII scores and memory and cognitive functioning, future work is needed to further explore the neurobiological mechanisms underlying the complex relationship between inflammation-related dietary behavior and memory and cognition.

Keywords

dietary inflammatory index; cognition; executive functioning; neuroscience; nutrition; obesity; population health

Introduction

Memory is an important constituent of higher-level cognition. Specifically, executive functioning is suggested to mechanistically influence, and be influenced by, numerous dimensions of memory, including episodic, working, and semantic memory.[1; 2] In terms of short and long-term memory, episodic memory refers to the memory of an event or an "episode". Working memory capacity and executive function share a common underlying executive attention that is strongly predictive of higher-level cognitive function, including episodic memory.[3] Executive function includes subcomponents of cognition, such as cognitive-related inhibition and reasoning. These parameters may help to facilitate basic cognitive functioning required to perform goal-directed behaviors (e.g., inhibiting and filtering distractive stimuli). Further, individuals with enhanced levels of executive function generally have the ability to maintain an appropriate mental state to fulfill a future goal,[4] which may include cognitive processes such as planning, filtering competing information, maintaining efforts despite distractions, and inhibiting goal-inconsistent responses.[5] Lastly, semantic memory involves retrieval of factual information that is learned over a period of time (e.g., the definition of a word)[6] and is not bound to any specific experience in which the memory was acquired.[7] Evaluation of factors influencing semantic memory is of particular importance as semantic functional MRI (fMRI) activation has been shown to serve as a better predictor of cognitive change when compared to episodic fMRI tasks.[8]

Emerging work suggests that obesity is associated with worse memory function. For example, chronic obesity may detrimentally influence memory function through morphological brain changes, insulin resistance, neuroinflammation, triglyceride metabolism, circulating levels of glucocorticoids, and cerebral metabolite concentrations.[9] In addition to obesity, research demonstrates that obesity-related diets, such as the "Western diet" (high in saturated fats and simple sugars), has been shown to correlate with impairments in learning and memory.[10; 11; 12; 13; 14] Further, some work suggests that such memory impairments may be diet-induced, as opposed to be driven by changes in adiposity.[15] For example, results from recent animal studies demonstrate that spatial and working

memory deficits are observable after only a few days of consuming a Western diet.[16] Human studies also indicate diets high in vegetables, fruit, fish, soy products may benefit cognitive functioning in older individuals.[17]

Existing observational work examined DII scores and cognitive function over time. This includes evidence for pro-inflammatory diets to correlate with incident cognitive impairment and dementia among older women,[18] as well as middle-aged men and women evaluated thirteen years following initial cognitive assessment.[19] Related work[19] has examined the association of DII on semantic memory and working memory, although episodic memory performance was not included as an outcome of interest,[19] which is a novel addition of our present study. We evaluated this topic further, by extending the investigation to include a nationally representative sample of US older adults, as this population is susceptible to age-related memory impairment.[20] Thus, the main purpose of this study was to examine the association between DII scores and a test battery of specific memory functions. Additionally, to comprehensively evaluate the association between DII and memory, we examined this potential association while considering various memory parameters, including episodic memory, working memory, and semantic memory.

Methods

Study Design and Participants

The National Health and Nutrition Examination Survey (NHANES) is an ongoing survey conducted by the Center for Disease Control and Prevention. NHANES employs a nationally represented sample of U.S. adults evaluated through a multistage, clustered probability design. Participants are initially interviewed in their homes and then, within 1–2 weeks, examined in a mobile examination center (MEC). Details of the NHANES methodology is available on the NHANES website (http://www.cdc.gov/nchs/nhanes.htm).

NHANES Procedures were approved by the National Center for Health Statistics institutional review board. Consent was obtained from all participants prior to data collection. Participant data from the 2011–2012 and 2013–2014 NHANES cycles were utilized, as these are the latest NHANES cycles with memory function data. The NHANES analytic sample included 1,723 older adults 60–85 years (only those in this age range were eligible for memory assessment) of age who did not have one or more of the following chronic diseases: congestive heart failure, coronary artery disease, heart attack, stroke, or physician-diagnosed diabetes.

Dietary Inflammatory Index (DII®)

Dietary intake was assessed using the 24-hour dietary recall interviews (24HR) that were validated by the Nutrition Methodology Working Group.[21] A single 24HR was used to calculate DII scores. The details of development of DII are described by Shivappa and colleagues.[22] High sensitivity c-reactive protein (CRP) measurements were used to examine construct validity of the DII in a longitudinal cohort using 24HR and 7-day dietary recalls. Subsequently, the new DII also was validated testing its effectiveness in four studies

among different populations with an extended number of inflammatory biomarkers (e.g., interleukin, IL-6, hs-CRP, and TNF-α).[23; 24; 25; 26; 27]

The DII consists of 45 food parameters which include various macro and micronutrients, flavonoids, spices and food items, each associated with an inflammatory effect score.[22] These 45 food parameters were based on findings contained in a total of 1,943 articles that were reviewed and scored for their associations with these inflammatory biomarkers (CRP, IL-1β, IL-4, IL-6, IL-10 and TNF-α). A global database (food consumption from eleven populations globally) representing global daily intake for each of the 45 parameters (i.e. foods, nutrients, and other food components) was used as standard dietary intake to calculate the DII. A standard mean for each parameter from the representative world database was subtracted from the actual individual exposure and divided by its standard deviation to generate Z scores. These Z scores were converted to proportions (minimizing effects of outliers/right- skewing). This value was then doubled and 1 was subtracted to achieve symmetrical distribution with values centered on 0. The resulting value was then multiplied by the corresponding inflammatory score derived from scoring the 1,943 research articles for each food parameter and summed across all food parameters, to obtain the overall DII. To control for the effect of total energy intake, the DII was calculated per 1,000 calories of food consumed, which requires using the energy-standardized version of the world database. For the present study, 26 of the 45 food parameters were available for DII calculation. Previous work indicated that there is no change in predictive ability of the DII in predicting inflammation when fewer food parameters are available (e.g., 26) compared to the full list of 45. In fact, rarely, if ever, do datasets have all available food parameters.[22] These foods included carbohydrate, protein, fat, alcohol, fiber, cholesterol, saturated fatty acid, mono-unsaturated fatty acid, poly-unsaturated fatty acid, niacin, thiamin, riboflavin, vitamin B12, vitamin B6, iron, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin D, vitamin E, folic acid, beta carotene, omega 6, and omega 3.

Memory Function

Several memory function assessments (episodic, semantic, and working memory/executive function) were employed, including the Consortium to Establish a Registry for Alzheimer's disease[28] (CERAD) Word Learning subset, the Animal Fluency test, and the Digit Symbol Substitution Test (DSST).

The CERAD Word Learning subset has been used in several major epidemiological studies with diverse racial and cultural communities.[29; 30; 31; 32] This test specifically assesses episodic memory and consists of three learning trials, along with a delay trial (i.e., fourth trial). For the learning trials, participants read aloud 10 unrelated words, one at a time, as they are presented on a computer screen. Following the 10th word, participants recalled as many words as possible. The order of the words changed across the three trials. The delayed trial occurred approximately 10-minutes after trial 1. The maximum score for each trial is 10.

The Animal Fluency test also has been employed in various epidemiologic cohorts, [33; 34; 35; 36; 37] assessing verbal fluency[38] and semantic-based memory function. In this

task, participants are asked to name as many animals as possible in one minute. One point was given for each named animal.

The DSST is a component of the Wechsler Adult Intelligence Test,[39] and has been used in large epidemiological and clinical studies.[40; 41; 42] The DSST relies on processing speed, sustained attention, and working memory, and is frequently used as a sensitive measure of frontal lobe executive function.[43; 44] The DSST was assessed using a paper-and-pencil format. At the top of the paper was a key containing 9 numbers paired with symbols. Participants had two minutes to copy the corresponding symbols in 133 boxes that adjoin the numbers. A score was given for each correct match, with maximum score of 133.

Statistical Analysis and Covariates

Analyses (Stata®, v. 12) accounted for the complex survey design employed in NHANES by utilizing sample weights, primary sampling units and strata via the Taylor series (linearization) method. Sample weights were re-weighted to account for the use of combined NHANES cycles. This was done by multiplying the 2-year cycles by 0.5. Information on the use of sample weights to generate population weighted estimates is available elsewhere.[50]

Multivariable linear regression analyses were fit. Analytical assumptions of linear regression were checked and confirmed not to be violated. Models were computed separately for each memory outcome. In each model, DII was categorized into quartiles (lowest quartile as referent; see Table 1 for the mean DII values across the quartiles), with covariates including: *age* (yrs; continuous), *sex* (male/female), *race-ethnicity* (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other), measured *body mass index* (kg/m^2; continuous), self-reported *smoking status* (never, former, current), self-reported average hours of *sleep* each night (hrs/night; continuous), self-reported engagement in leisure-time moderate-to-vigorous *physical activity* (min/week) assessed from the Global Physical Activity Questionnaire,[45; 46] and PHQ-9 assessed *depression symptomology* (range = 0–27; continuous). Statistical significance was established as a nominal alpha of 0.05.

Results

Table 1 displays the demographic characteristics of the study variables. Participants, on average, were 68.4 years, with the sample similarly distributed across sex (58% female). Participants with a higher DII (i.e., 4th quartile) were more likely to be male, be a smoker, had a higher body mass index, and engaged in less physical activity.

In an adjusted model, and when DII was expressed as a continuous variable, DII was not statistically significantly associated with Trial 1 (β = −.02; 95% CI: −.09, .03), Trial 3 (β = −.01; 95% CI: −.07, .05) or the delay Trial (β = −.06; 95% CI: −.15, .01) of the CERAD, but was significantly associated with Trial 2 of the CERAD (β = −.08; 95% CI: −.13, −.01), the Animal Fluency test (β = −.24; 95% CI: −.42, −.06) and the DSST (β = −.64; 95% CI: −1.16, −.13).

Table 2 displays the regression results examining the association between DII scores (categorized into quartiles) and memory function. Results were similar for the unadjusted

and adjusted models. Additionally, there was evidence of consistent inverse associations between DII scores and the different memory parameters. For the episodic memory (CERAD Word Learning), those in the 4th (i.e., more pro-inflammatory) vs. 1st (i.e., more anti-inflammatory) DII quartile recalled fewer words during the 10-min delay assessment ($b_{adjusted}$ = −.39; 95% CI: −.79, .00). Similarly, for semantic-based memory (Animal Fluency Test), those in the 4th vs. 1st DII quartile listed fewer animal names ($b_{adjusted}$ = −1.18; 95% CI: −2.17, −.20). Lastly, for the executive function and working-memory assessment (DSST), those in the 4th vs. 1st DII quartile correctly matched fewer paired symbols ($b_{adjusted}$ = −2.80; 95% CI: −5.58, −.02). Notably, there was no evidence of an interaction effect of sex and DII on any of the memory outcomes (results not shown).

Discussion

The purpose of this study was to examine the association between DII scores and a test battery of specific memory functions. The main finding of our study was that higher DII scores were associated with worse episodic memory, working memory, and semantic memory. Notably, however, DII was not consistently associated with the first three learning trials of the CERAD, but was significantly associated with the delayed trial of the CERAD. This suggests that dietary inflammation, as measured by the DII, may be less related to memory encoding, but may have a larger influence on memory consolidation. Of course, future work is needed to evaluate this speculation.

Reduced cognitive performance has been evidenced in rats consuming an energy-dense, Western-style diet.[10] Notably, cognitive functioning diminished following only three days of this high-fat dietary regimen, highlighting the plausible risk for deleterious cognitive outcomes to precede weight gain. This is a meaningful outcome, as not only are weight gain and chronic obesity associated with cognitive impairment, but acute deleterious changes in dietary practices may accelerate this risk of decline.[10]

Although caloric requirements can be met by consuming a variety of healthful nutrients, Americans often consume foods high in refined carbohydrates and saturated fat.[47; 48] These foods are known to trigger dopaminergic reward pathways, strengthening learned associations between pleasurable food stimuli and immediate reinforcement.[48; 49] Initially, ingestion of fatty and/or sugary meals increases the rate of dopaminergic firing, governed by the ventral tegmental area, along with dopamine release from the nucleus accumbens. Habitual intake of foods common to the Western diet, habituates the dopamine reward response to manifest even during the *anticipation* of experiencing food rewards.[50] The hippocampus, an important subcortical memory structure, is also a key neuromodulator involved in the regulation of energy intake. Studies evaluating the influence of amnesic pathology in humans have shown that excessive eating behaviors may be accelerated following damage to the hippocampus.[51; 52; 53] Other animal research suggests that hippocampal-dependent, episodic memory (including flexible memory) impairment may be attenuated by engaging in regular physical activity, despite concurrent consumption of a high-fat diet.[54] This finding lends further credence to the potential efficacy of physical activity to preserve memory functioning, counteracting diet-associated deficits in acute and delayed recall, attention, and processing speed.[16; 55; 56] Our findings, however, demonstrate

an association between DII and memory function, independent of self-reported physical activity behavior.

It has been suggested that consumption of inflammatory-related, high-fat, high-sugar diets may induce both transient and sustained neurological deficits, particularly dependent upon hippocampal and prefrontal cortex (PFC) function.[57] Inhibitory control and global memory function may suffer as a result of neural disturbances within these regions. Coupled with a heightened dopamine response, impaired inhibition and memory functioning contribute to poor appetite regulation via incongruous hunger cues,[58] which may lead to overeating and continuation of negative dietary behaviors. This cyclical response has been observed directly in rats that demonstrate an inability to regulate hunger signals, becoming hyperphagic following hippocampal lesions.[53; 59; 60; 61]

Regarding the crucial importance for adequate functioning of the hippocampus and PFC to remain intact, the hemispheric encoding retrieval asymmetry (HERA) model posits these structures are responsible for distinct roles within the complex domain of memory mechanisms. Retrieval of semantic information is governed by the left PFC, whereas the right prefrontal cortex directs retrieval of episodic memory.[62] The Trace Transformation theory (TTT) proposes acute memory processes are encoded and organized in the hippocampus, reach neocortical storage, and may then be transformed into shared, hippocampal-neocortical representations.[63; 64] Taken together, the differential impact of dietary behaviors on these (and other) highly-integrated structures warrants continued scientific exploration. Dietary inflammation must be regarded as a preventable function of poor diet. Therefore, increasing the quality and quantity of reputable research on this topic, will do much to expand empirical knowledge of the downstream impact of the obesity epidemic. High-fat, high-sugar diets may impart neural and systemic risks associated with weight gain, memory impairment, and cognitive dysfunction.[48; 65] However, recent work admonishes scientists to consider variable inflammatory-induced metabolic and cognitive responses specific to white, beige, and brown adipose tissue[66] when attempting to explain the specific correlates of body weight and cognition, as the relationship may be more nuanced than expected.[67] Nevertheless, our findings that higher DII scores (i.e. consistent with greater diet-related inflammation) were associated with worse episodic memory, working memory, and semantic memory are noteworthy, and should prompt continued research on this exigent health concern. Such work should continue to explore the specific dietary-related neuro-inflammatory effects on key cellular pathways (e.g., long-term potentiation) that subserve memory function. For example, emerging work suggests reduced synaptic potentiation, long-term potentiation, and glutamate release are suggested to be associated with IL-1 mediated inflammatory responses.[68] Pro-inflammatory cytokines, such as IL-1, are found in high concentrations in the hippocampus,[69] and may exert profound negative effects on memory and cognition. Exogenously applied IL-1 can inhibit calcium influx,[70] protein kinase A (PKA),[70] and release of acetylcholine[71] and glutamate[72; 73] in the hippocampus, all of which play a key role in the cellular basis of episodic memory.

Memory deficits, impaired neuronal growth and proliferation, and inhibited brain-derived neurotrophic factor (BDNF) activity also are driven by diet-induced endothelial cell

dysfunction, and subsequent IL-1 release across the blood-brain barrier. Further, neuroinflammation linked with microglial phenotypic changes engendered by chronic systemic inflammation may limit the efficiency of long-term hippocampal potentiation.[47; 74]

Diet-induced obesity also has been shown to impair dopaminergic signaling.[75] Diet-associated adiposity may impair memory as dopamine plays an important role in memory function.[76] For example, dopamine receptor-mediated signals (e.g., via D1 and D2 receptors) are important in facilitating long-term potentiation,[77; 78] a critical cellular basis of memory function (particularly episodic memory).[79] Dopamine regulation of long-term potentiation may occur via the D1/cAMP/PKA pathway, where the D1 receptor coupled to adenylate cyclase (AC) increases AC activity.[76] This leads to the formation of cAMP that activates PKA, which in turn can phosphorylate transcription factors (e.g., CREB) as well as phosphorylate both AMPA and NMDA receptors,[76] key receptors in memory-related long-term potentiation.

A limitation of this investigation was our use of a single measure of dietary intake, assessed across a time-period of twenty-four hours. However, this measure has been validated (i.e., correlated with other markers of inflammation) in previous research in large populations,[23; 24; 25; 26; 27] and, thus, was an appropriate method to estimate DII for the purposes of the present study. Another limitation is that the NHANES memory assessments, particularly the DSST, does not exclusively measure memory function, as it also evaluates other sub-cognitive parameters such as cognitive processing speed and executive function. However, the consistent findings of an association between DII and the three memory-related assessments provides credence to these observations. Additionally, NHANES did not collect data on cognitive impairment or neurocognitive disorders; thus, we were unable to take this into account when interpreting our findings. Further, like all epidemiological studies, it is not possible to fully discount the potential effects of residual confounding bias. We are also not able to infer causality of our observed associations given the cross-sectional design of our study. Thus, we cannot discount the potential reverse causality, or possible bi-directionally of DII and memory function. Lastly, based on the available NHANES data, we were only able to include 26 of the original 45 parameters when calculating DII. Thus, our calculated DII may be an underestimate of the participant's true DII, and as a result, our observed association between DII and memory may be underestimated. To our knowledge, this is the first study assessing older US men and women ages 60+ from a nationally representative sample. In addition, as no studies have explored the specific relationship between DII on a multitude of memory parameters, this paper is a robust first step to more comprehensive research. Future work should track dietary behavior over multiple days to provide a more inclusive representation of changes in dietary behavior across time.

In conclusion, we observed a consistent inverse association between DII and various memory types. Future experimental work confirming our findings are warranted. Our findings underscore the importance of eating an anti-inflammatory diet, not only for cardiovascular reasons, but for cognitive purposes as well. Future work investigating potential molecular mediators of the DII-memory relationship is also warranted.

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Table 1

Weighed characteristics of the study variables (N=1,723), NHANES, 2011–2014.

Variable	Point Estimate (SE)				
	Entire Sample	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile
Age, mean years	68.4 (0.2)	69.3 (0.4)	68.7 (0.3)	67.5 (0.4)	68.2 (0.5)
Gender, % Female	58.4	67.4	57.6	56.2	51.9
Race-Ethnicity, % non-Hispanic White	81.8	82.6	81.9	81.4	81.4
Smoking Status, %					
Every day	8.2	2.9	5.9	8.3	15.3
Some days	1.3	0.3	1.8	0.8	2.2
Former smoker	37.1	40.7	38.1	35.4	33.8
Never smoker	53.6	55.9	54.0	55.3	48.5
Body Mass Index, mean kg/m^2	28.3 (0.2)	27.1 (0.2)	28.3 (0.3)	28.8 (0.4)	28.9 (0.3)
Sleep, hrs/night	7.2 (0.03)	7.2 (0.1)	7.1 (0.1)	7.2 (0.1)	7.1 (0.1)
Depression, mean PHQ-9	2.4 (0.1)	2.3 (0.2)	2.1 (0.1)	2.2 (0.1)	2.8 (0.2)
Moderate-to-Vigorous Physical Activity, mean min/week	138.1 (8.7)	170.9 (15.8)	151.1 (16.5)	128.8 (15.2)	98.4 (10.6)
Dietary Inflammatory Index, mean	−0.25 (0.07)	−2.79 (0.05)	−0.78 (0.02)	0.56 (0.02)	2.21 (0.03)
CERAD Word Learning					
Trial 1, mean words	5.2 (0.1)	5.2 (0.1)	5.1 (0.1)	5.3 (0.1)	5.0 (0.1)
Trial 2, mean words	7.2 (0.1)	7.3 (0.1)	7.2 (0.1)	7.2 (0.1)	6.9 (0.1)
Trial 3, mean words	8.0 (0.1)	7.9 (0.1)	8.0 (0.1)	7.9 (0.1)	7.9 (0.1)
Delay Trial, mean words	6.6 (0.1)	6.7 (0.1)	6.5 (0.2)	6.6 (0.1)	6.3 (0.1)
Animal Fluency, mean number of animals	18.9 (0.2)	19.4 (0.4)	19.1 (0.3)	18.7 (0.3)	18.1 (0.3)
Digit Symbol Substitution Test, mean	55.9 (0.6)	57.2 (1.1)	56.4 (1.1)	56.1 (1.2)	53.3 (1.0)

Table 2

Regression results examining association between DII and memory function (N=1,723), NHANES, 2011–2014.

	Unadjusted		Adjusted	
CERAD Word Learning	**b**	**95% CI**	**b**	**95% CI**
Trial 1				
DII Q2 vs. Q1	−.03	−.34, .27	−.03	−.30, .24
DII Q3 vs. Q1	.09	−.26, .44	.01	−.26, .29
DII Q4 vs. Q1	−.16	−.50, .18	−.11	−.44, .21
Trial 2				
DII Q2 vs. Q1	−.10	−.42, .20	−.09	−.37, .17
DII Q3 vs. Q1	−.08	−.42, .25	−.16	−.43, .10
DII Q4 vs. Q1	**−.34**	**−.67, −.01**	−.30	−.66, .05
Trial 3				
DII Q2 vs. Q1	.16	−.20, 54	.18	−.18, .55
DII Q3 vs. Q1	.01	−.31, .34	−.04	−.32, .23
DII Q4 vs. Q1	.03	−.36, .42	.07	−.32, .46
Sum of Trials 1–3				
DII Q2 vs. Q1	.01	−.88, .92	.05	−.76, .88
DII Q3 vs. Q1	.02	−.87, .92	−.19	−.87, .48
DII Q4 vs. Q1	−.47	−1.40, .46	−.34	−1.28, .59
Delay Trial				
DII Q2 vs. Q1	−.17	−.65, .29	−.18	−.59, .22
DII Q3 vs. Q1	−.02	−.43, .39	−.16	−.53, .20
DII Q4 vs. Q1	**−.39**	**−.76, −.03**	**−.39**	**−.79, .00**
Animal Fluency				
DII Q2 vs. Q1	−.23	−1.36, .90	−.33	−1.21, .54
DII Q3 vs. Q1	−.66	−1.68, .35	**−1.00**	**−1.89, −.12**
DII Q4 vs. Q1	**−1.22**	**−2.34, −.10**	**−1.18**	**−2.17, −.20**
DSST				
DII Q2 vs. Q1	−.80	−3.88, 2.27	−.66	−3.15, 1.82
DII Q3 vs. Q1	−1.16	−4.73, 2.40	−1.84	−4.68, .99
DII Q4 vs. Q1	**−3.93**	**−6.86, −1.01**	**−2.80**	**−5.58, −.02**

DSST, Digit Symbol Substitution Test
Q, Quartile

Bold text indicates statistical significance (P<0.05)

In the adjusted model, covariates included age (yrs; continuous), sex (male/female), race-ethnicity (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other), measured body mass index (kg/m^2; continuous), self-reported smoking status (never, former, current), self-reported average hours of sleep each night (hrs/night; continuous), self-reported engagement in leisure-time moderate-to-vigorous physical activity (min/week) assessed from the Global Physical Activity Questionnaire, and PHQ-9 assessed depression symptomology (range = 0–27; continuous).