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Association of Healthy Lifestyle Behaviors with Cognitive Functions

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Bachelor of Pharmacy

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An abstract of

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Abstract

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By Srividya Vempati

Background: Due to the lack of effective pharmacological treatment for dementia, an increasing public health focus is on promoting behavioral changes in regard to modifiable risk factors. This study explores the effect of a new health metric, the Healthy Lifestyle Index Score(HeLIS) comprising of six modifiable health behaviors – diet, sleep, stress, alcohol consumption, smoking status, and physical activity on cognitive function.

Methods: Baseline data from 69 participants of the VAScular ContribUtors to prodromaL AlzheimeR's disease(VASCULAR) cohort study was used. Information regarding the six health behaviors was recorded through self-administered and validated questionnaires. Validated cognitive tests were used to measure cognitive function, namely language function, attention, episodic memory, and executive function. Based on public health recommendations, each component was divided into groups and assigned a score of 0,1, or 2, reflecting poor, intermediate, and ideal levels, respectively. HeLIS was obtained by summating individual components, ranging from 0-10, with a higher score implying better adherence to healthy behaviors. Crude and adjusted linear regression analyses were conducted to analyze the association between HeLIS and cognitive function. The association of individual HeLIS components with cognitive function was conducted using linear regression.

Results: The mean age of the population was 64 years, comprising African Americans(39%) and Whites(61%). Higher HeLIS showed significantly better executive functioning(β= -10.08, 95% CI: -18.34, -1.82) and language performance (β=0.18, 95%CI: 0.002, 0.35), although no significant association was seen with attention and episodic memory. Non-smokers performed significantly better in executive function test(β=-58.9, 95% CI: -100.33, -17.46), memory (β = 10.49, 95%CI: 2.55, 18.43) and language (β = 1.27, 95%CI: 0.4, 2.14). Low-stress levels showed significantly improved performance in all the domains assessed.

Conclusion: Our results suggest that better adherence to healthy lifestyle behaviors improves cognitive functioning, especially executive function, which is an essential domain engaged in activities of daily living(ADL). Our study also adds to the existing body of literature, the impact of low-stress levels on cognitive abilities. Findings from similar studies in the future could inform policies to promote healthy living, to reduce the burden of dementia among the aged population.

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Introduction

With the increase in global life expectancy, the burden of dementia is also on the rise. By 2050, the number of people living with dementia is predicted to cross 150 million, nearly three times that in 2019[1]. While dementia is associated with memory loss and difficulty performing everyday tasks, mild cognitive impairment (MCI) presents decreased memory and cognition but no impairment in daily functioning. MCI has been regarded as early-stage dementia, with a conversion rate varying from 2% to 31%, as per one review[2]. Neurocognitive domains associated with dementia and cognitive impairment include memory, attention, language, visuospatial functions, and executive functions [3]. Various neuropsychological assessment methods help diagnose various types of dementia and other related disorders, like MCI. A long-term impairment in a single cognitive domain and disturbance in daily functioning typically characterizes dementia. [4]. Dementia can be further classified based on the associated physiological changes in the brain into Alzheimer's disease, Lewy Body Dementia, Vascular Dementia, and Frontotemporal Dementia[5].

Current pharmacological treatments only provide symptomatic relief or delay cognitive decline; they do not treat or reverse pathophysiological changes[6]. Non-pharmacological approaches include behavioral therapy and psychotherapy[7]. Due to the lack of effective pharmacological interventions, it is essential to stress the importance of incorporating healthy lifestyle behaviors, which have been proven to be effective with cardiometabolic disorders, including diabetes and kidney disorders[8]–[10]. Life's Simple Seven(LS7), a health metric comprising seven modifiable risk factors for ideal cardiovascular health, was prescribed by the American Heart Association in 2010 to promote lifestyle behavior change[11]. Many studies have been conducted assessing adherence to LS7 and improved performance among cognitive domains[12]–[16]. However, few studies have assessed the association between the score and cognitive domains since adding sleep to the health metric, now known as Life's Essential 8[17].

Thus, this study focuses on investigating the association between a new composite lifestyle metric, **He**althy **L**ifestyle **I**ndex **S**core (HeLIS) metric, comprising six modifiable health behaviors (i.e., physical activity, diet, smoking, stress, alcohol, and sleep on overall cognition and specific domains of executive function, language, episodic memory, and attention.

Methods

Study population

Data for this study was obtained from 69 participants who were enrolled in the VASCULAR (VAScular ContribUtors to prodromaL AlzheimeR's disease) study. The VASCULAR study is a case-control study (n = 350) enrolling participants 50 years or older with MCI (n = 175) and without MCI (n = 175) to investigate the role of vascular disease in Alzheimer's disease[18].

Information about lifestyle habits was obtained through validated socio-behavioral questionnaires administered at baseline.

Exposure

Physical activity

Physical activity is measured through the Physical Activity Scale for the Elderly (PASE), that quantifies physical activity typically used in studies among people who are 65 years and older[19]. The survey consists of 12 questions capturing the frequency, duration, and intensity of leisure, work, and household activities over one week [20], with scores ranging from 0 to 793. Higher scores indicate more physical activity.

Based on the distribution of PASE scores in the dataset, we divided the data into tertiles and assigned a score of 2 to PASE scores in the highest tertile, 1 to the intermediate tertile, and 0 to the lowest tertile(See Table 1).

Diet

The diet score comprised data from 4 beneficial Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) food groups – fruits, vegetables, fish, and whole grains and one unhealthy food group – sweet consumption[21]. The MIND diet is a hybrid of two recommended health diets – the Mediterranean diet and the Dietary Approaches to Stop Hypertension(DASH) diet. Both diets are associated with improvements in to have cardiovascular and cognitive health[22]–[24]. Quantities of consumption were obtained through questions that addressed the following: “How many cups of fruit do you eat in a day?”, “How many cups of vegetables do you eat in a day?”, “How many servings of fish do you eat in a week?”, “How many servings of whole grain do you eat in a week?”, “How many beverages with added sugar do you drink a week?”.

For fruit/berries consumption, a score of 1 was assigned if at least two fruits were consumed daily and 0 if otherwise. If at least one vegetable was consumed daily, a score of 1 was coded and 0 if not. A score of 1 was assigned if at least one meal comprising fish was consumed and 0 if not. If at least three servings of whole grains per week are consumed, a score of 1 was assigned and 0 if not. A score of 1 was assigned for sweet consumption if less than five servings of sweetened products were consumed weekly and 0 if otherwise. The assignment of scores was based on modifications of MIND recommendations to apply to the definition of the variables in the dataset. Summing all the individual scores, with the highest possible score being 5(implying healthy food choices), the score was further divided into two groups – scores below 4 were given a diet score of 0, and scores above or equal to 4 were assigned a diet score of 1.

Sleep

Sleep duration was assessed through the Pittsburgh Sleep Quality Index[25]. Values were rounded to the nearest whole number. If the number of daily hours of sleep was between (and including) 7 and 8, a score of 2 was assigned. For daily hours of sleep equal to 6 or 9, a score of 1 was given; for less than 6 hours or greater than 9 hours of sleep obtained, a score of 0 was assigned. The cutoffs have been based on previous literature regarding the impact of sleep on cognition[26]–[30].

Stress

Stress was assessed through the Perceived Stress Score(PSS) questionnaire, a validated stress questionnaire commonly used in studies on cognition and dementia[31]. The total score ranges from 0 to 40, with a higher score implying greater stress. If the PSS score was below 13, an ideal score of 2 was assigned. For a score between 14 and 26, a score of 1 was assigned, and a score of 0 was assigned if the PSS score was between 27 and 40.

Smoking status

A questionnaire that inquired about one’s current smoking status was administered to determine smoking status. For ‘yes’ to being a current smoker, a score of 0 was assigned, and for ‘no’ to being a current smoker, a score of 1 was assigned.

Alcohol consumption

Through a self-administered questionnaire, alcohol consumption habits was recorded. For those who reported they do not consume alcohol, a score of 1 was assigned. If the daily consumption of drinks was at least 2 for males and at least 1 for females, a score of 0 was assigned. For males consuming less than 2 drinks daily and females consuming less than 1 drink daily, a score of 2 was assigned[32].

HELIS score

The HELIS score was obtained as a sum of scores assigned to individual lifestyle categories. The scores ranged from 0 to 10, with a higher score indicating greater adherence to healthy lifestyle habits(See Table 1).

Covariates

Covariates included in the analysis were age, sex, and race. Age was defined as the age at the date of consent. Racial groups included in the study were African American and White populations.

Outcome measures

The cognitive domains assessed were executive function, attention, language, and episodic memory. To measure executive functioning, the Trail Making Test was utilized in which particularly the difference between the time taken to complete Part B(TMT-B) and Part A(TMT-A) (i.e., TMTB-A) was assessed [33]. The Digit Span Backward (DSB) Test was utilized to assess attention and working memory[34]. To understand episodic memory, verbal learning abilities, and delayed recognition, the revised version of the Hopkins Verbal Learning Test was used[35]. The 15-item Boston Naming Test(BNT) was used to assess language and word retrieval abilities through visual confrontation naming[36]. The Montreal cognitive assessment is a validated screening test for MCI measuring global cognition[37]. It assesses various subdomains of cognition, such as short-term memory, executive function, visuospatial abilities, attention and working memory(Table 2).

Statistical Analysis

Only completed data for exposure, covariates, and outcomes were included in the analysis. Descriptive statistics were calculated for continuous and categorical variables. Interaction assessment was conducted to investigate if the covariates gender and race modified the association of interest. Multivariate regression analysis assessed the association between cognitive performance outcomes and HeLIS. The first model considered was unadjusted and gave a crude estimate. Multiple models were tested, adjusting for age, race, and gender. Adjusted models were tested for effect modification by race and sex. Individual HeLIS components were also tested for their association with cognitive outcomes included. All analyses were conducted using SAS 9.4 (Cary, NC; SAS Institute Inc, Cary, NC, USA).

Results

The mean age of the population was 64 years old. Majority of the participants were White (61%) and female (61%). The population reported a mean TMTB-A difference of approximately 62 seconds and repeated at least 7 digits on the DSB in the reverse order correctly. The average percentage retention of words following the 3 learning and delayed recall trial was 47%. The population performed well on the BNT, averaging 14 out of a maximum of 15. (See Table 3)

Individuals in the population sample reported a greater prevalence of poor alcohol consumption habits (59%). Sleep, in terms of sleep duration, showed the highest prevalence in the ideal group. Nearly 90% of the participants were non-smokers, and 83% adhered to a healthy diet per MIND food groups. There was an equal distribution of subjects in each tertile of physical activity. Most subjects reported a PSS score between 14 and 26 (64%), and only 12 out of 69 participants reported a PSS score below 13(See Figure 1).

As age increased by one year, HeLIS increased by 0.023 units (95% CI: -0.02, 0.07). Men were more likely than women to report a higher HeLIS, implying greater adherence to healthy lifestyle choices (Mean difference between males and females=0.63, 95%CI -0.12, 1.38). Whites were more likely to show better adherence to healthy behaviors than Blacks, reporting a higher HeLIS (Mean difference between Whites and Blacks= 1.01; 95% CI, 0.28, 1.74), which was significant(See Table 4).

The unadjusted model showed a significant negative association between the TMTB-A time and HeLIS (β= -10.08, 95% CI: -18.34, -1.82). After adjusting for subject race, age, and sex, TMTB-A decreased by 10.14 seconds for every one-unit increase in HeLIS (95% CI: -18.57, -1.71). Attention was positively associated with HeLIS with an average increase in performance on the DSB by 0.16 units for every one-unit increase on the HeLIS metric (95% CI: -0.27, 0.58). Adjusted analysis showed an average rise in DSB score by 0.233 for every one unit increase in HeLIS (95% CI: -0.23, 0.69). Performance on the

HVLT-R also improved as HeLIS increased by 1 unit, for both crude (β=1.28, 95% CI:-0.33, 2.89) and adjusted analyses (β=1.25, 95% CI: -0.49, 3)(See Table 5).

To ascertain if the magnitude of the above explored associations differed by sex or race, an interaction assessment was carried out. The coefficient of the interaction terms (HeLIS * sex/HeLIS * race) have been reported in Table 6. There is no evidence of statistically significant interaction, as indicated by the p-values(See Table 6).

Alcohol: With increasing alcohol score, cognitive performance in all domains decreased. This decrease was consistent comparing both the ideal and intermediate tertiles with the lowest tertile as reference. Global cognition, as indicated by MoCA score declined as well, with the score decreasing by 2.05(95%CI: -3.99, -0.11) units going from poor to intermediate alcohol consumption and by 3.03(95%CI:-6.24, 0.17) units from alcohol score 0 to alcohol score 2 comparing the ideal alcohol group(See Table 7a).

Smoking status: Compared to smokers, non-smokers showed a statistically significant improvement in 3 out of 4 domains, namely executive function (β=-58.9, 95% CI: -100.33, -17.46), memory (β = 10.49, 95%CI: 2.55, 18.43) and language (β = 1.27, 95%CI: 0.4, 2.14). Non-smokers reported better global cognition compared to smokers, with MoCA score improving by 2 units (95%CI: -0.91, 5.09)(See Table 7b).

Diet: The mean TMTB-A score decreased by 8.67s(95%CI=-43.53, 26.2), moving from those in the poor diet group to those in the ideal diet group. Memory improved slightly but was insignificant (β = 2.17, 95%CI: -4.45, 8.8). There was no change in language performance between the two diet groups (β=0). Performance on the DSB decreased from the poor diet group to the ideal diet group by 0.09 units (95% CI: -1.82, 1.53). Global cognition improved with better dietary adherence, by 1.65 units on the MoCA test (95%CI: -0.74, 4.04)(See Table 7c).

Stress: Both the ideal (β= 1.03, 95%CI: 0.14, 1.91) and intermediate(β= 0.81, 95%CI: 0.10, 1.51)tertiles of stress score performed significantly better than the poor tertile on the Boston Naming Test. All domains showed significant performance improvement when comparing the intermediate stress tertile with the poor tertile. Global cognition also improved from poor to intermediate stress groups (β=1.54, 95%CI: -0.85, 3.92) and from poor to ideal stress groups (β = 2.26, 95%CI:-0.77, 5.28)(See Table 7d)

Sleep: The mean TMTB-A score decreased by 21.38s(95%CI: -60.44, 17.67) while moving from the lowest to the ideal sleep tertile and by 4.91s(95%CI: -46.3, 36.48) comparing the poor sleep tertile with the intermediate sleep tertile. HVLT-R showed improvement moving from the poor sleep tertile to intermediate tertile(β=6.89, 95%CI:-0.89, 14.65) and comparing the ideal sleep tertile with the poor sleep tertile(β= 6.74, 95%CI:-0.6, 14.07).BNT performance increased for the intermediate sleep tertile(β=0.73, 95%CI: 0.13,1.59) and ideal sleep tertile(β=0.68, 95%CI:-0.13, 1.49) with the poor sleep tertile as reference. Those in the intermediate sleep tertile (β=0.13, 95%CI:-1.92, 2.18) and ideal sleep tertile(β =0.95, 95%CI:-0.98, 2.88) performed better on the DST compared with those in the poor sleep tertile(See Table 7e).

Physical activity: TMTB-A decreased on average by 37.35s(95%CI: -68.72, -5.98), comparing the executive performance of those in the ideal tertile of physical activity with those in the poor tertile of physical activity and by 19.18s(95%CI: -50.54, 12.19) moving to the intermediate tertile from the poor tertile of physical activity. Those in the ideal physical activity tertile improved performance compared with those in the poor tertile in both episodic memory (β=2.09, 95%CI: -5.06, 8.23) and language (β=0.48, 95%CI: -0.2, 1.16). The improving trend was also observed comparing the cognitive performance of the intermediate physical activity tertile to the poor physical activity tertile in the HVLT-R test (β=3.96, 95%CI: -2.19, 10.1) and language(β=0.30, 95%CI: -0.37, 0.98). Performance on the DSB, however, showed a decrease with the poor physical activity tertile as reference for both the ideal (β=-0.13, 95%CI: -1.74, 1.48) and intermediate (β= -0.48, 95%CI: -2.09, 1.13) physical activity tertiles(See Table 7f)

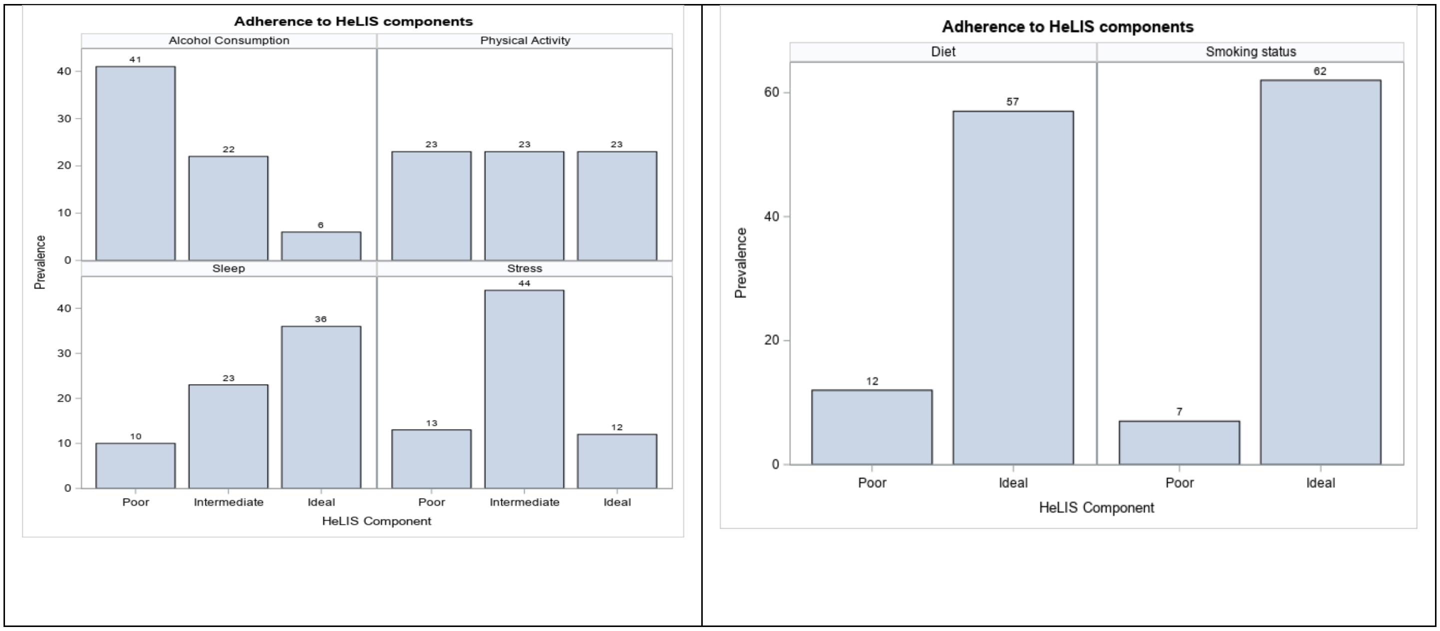

Figure 1. Individual HeLIS components distribution

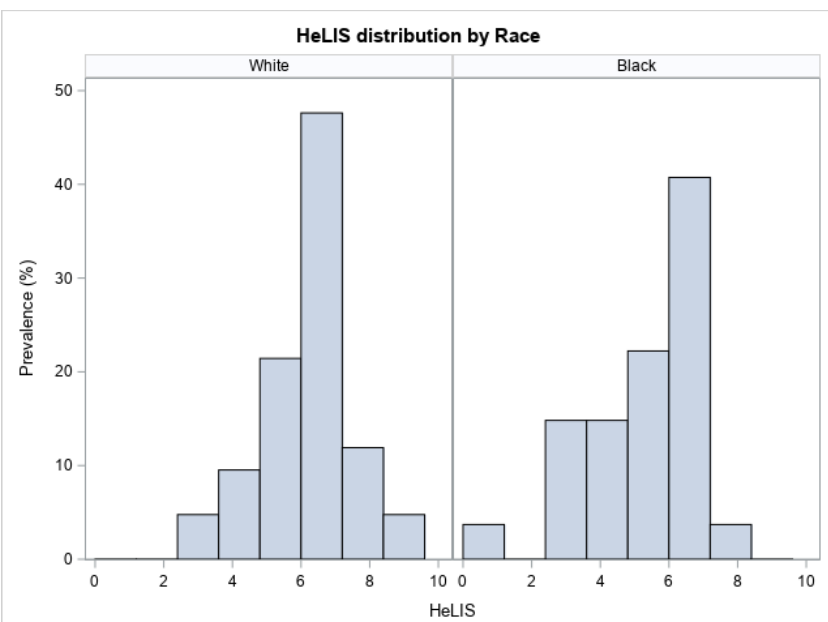

Figure 2. HeLIS distribution by race

Discussion

Among age, sex, and race, only race was significantly associated with HeLIS, with Whites showing greater adherence to healthy lifestyle behaviors than African Americans(See Figure 2).Executive function (crude and adjusted model) and language(crude model) showed significant improvement with better adherence to HeLIS components.

Individual component association of HeLIS with cognitive outcomes showed non-smoking status and intermediate stress levels to be significantly associated with improved cognitive performance. Non-smokers reported better performance on TMT, BNT and HVLT-R. Further, low stress levels were significantly associated with improvement in language function. These findings add to the existing body of literature investigating the impact of stress[29], [38]–[41] and smoking on cognition[42], [43]. The role of chronic high stress levels in cognitive decline could be explained by the impact on the hippocampus, which plays a crucial role in memory[44]. Another well researched theory is that stress tends to impact cognitive performance by increasing cognitive resources utilization to deal with the stressor rather than on cognitive tasks[45]. The exact mechanism by which smoking causes cognitive decline is not clear[46], but a plausible explanation for smoking being negatively associated is due to the role of tobacco smoke in causing oxidative stress, increasing the risk significantly for Alzheimer's[47] Ideal physical activity was also seen to improve executive function. In previous studies, physical activity is associated with improved mental acuity among children [48], normal adults, and adults with mild cognitive impairment. Among older adults, the benefit of aerobic exercise was most significant in executive function[49]. Dementia is associated with a loss of physical function and muscle strength to perform everyday functions and increased falls, increasing the risk of serious injuries [50].

The only individual component showing inconsistencies with previous studies was alcohol consumption, which showed a reverse, although not a significant trend, where excess alcohol consumption resulted in improved executive function. Previous studies showed the protective influence of alcohol, with some studies reporting no effect and very few purporting a negative association[51].

Considering HeLIS, this study's findings are consistent with previous studies investigating clusters/scores assigned to lifestyle behaviors with cognitive outcomes. A 13-year longitudinal study investigated the association between clustered midlife lifestyle choices and late cognitive functioning and showed a negative association between cognitive performance and increasing unhealthy lifestyle choices[52]. Another study examining the association between midlife Life’s Simple Seven scores and cognition showed higher scores leading to reduced cognitive decline among the Atherosclerosis Risk in Communities Study(ARIC) cohort, which was stronger in Whites than Blacks[13].

Potential limitations in the present study include the small sample size(n=69), which limited our statistical power. Since a greater portion of the exposure data is self-reported, this could be a source of information bias. A study showing that health behaviors promote executive functioning also investigated a positive feedback loop that results in sustained healthy behaviors due to improved executive function, which is crucial in decision-making [53]. Our study is also cross-sectional, the association and bidirectionality between cognition and lifestyle habits can be better understood and validated in a future longitudinal study. It could also better track changes in lifestyle behaviors and their impact on cognition. HeLIS would be more holistic if data were made available on social support and social engagement, which are known to be associated with improved cognitive outcomes[54]–[56].

Public Health Implications

Our investigation shows promise since it finds that healthy lifestyle can improve executive function performance, initiating a positive feedback leading to long term adherence to healthy behaviors, reducing the expected rise of the ‘silent epidemic’[57]. The simplicity of such metrics improves acceptability among the public since it presents complex clinical findings in a more understandable way to the ordinary person. Especially for a disease like dementia and Alzheimer’s disease, with no effective pharmacological therapies and a considerable disease incidence in older populations, it is essential to stress the importance of incorporating healthy lifestyle behaviors, to slow down cognitive decline and prevent it if adopted early. Future directions from this study include education programs to promote awareness about the protective effect of adopting healthy lifestyle habits on cognitive health. Through effective policies, lifestyle modifications can be strongly recommended to achieve a healthier population with improved cognitive health and reduce the burden of dementia.

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Tables

Table 1. HeLIS component scoring definitions

HeLIS component	**Levels**	**Score**	**Description**
Physical Activity	Ideal	2	Highest tertile of PASE
	Intermediate	1	Middle tertile of PASE
	Poor	0	Lowest tertile of PASE
Stress	Ideal	2	PSS 0-13
	Intermediate	1	PSS 14-26
	Poor	0	PSS 27-40

Sleep	Ideal	2	7-8 hours of sleep daily
	Intermediate	1	6 or 9 hours of sleep daily
	Poor	0	Less than 6 or greater than 9 hours of sleep daily
Alcohol Consumption	Ideal	2	Less than 2 drinks for men or less than 1 drink for women
	Intermediate	1	No alcohol consumption
	Poor	0	Daily consumption of more than 2 drinks for men or more than 1 drink for women
Smoking	Ideal	1	Non-smokers
	Poor	0	Current smokers
Diet*	Ideal	1	Adherence to 4 or more MIND food groups
	Poor	0	Adherence to less than 4 MIND food groups

*MIND food groups: Adherence= At least 2 fruits per day; at least one vegetable daily; at least 1 fish meal per week; at least 3 servings of whole grains per week; less than 5 servings of sweetened products

Table 2. Cognitive domains, tests, and outcome descriptions

DOMAIN	TEST	OUTCOME DESCRIPTION	WHAT IS CONSIDERED A GOOD OUTCOME?

EXECUTIVE FUNCTION	Trail Making Test (TMT)	TMTB-A: Difference in time taken to complete Part B and Part A	Lower TMTB-A is indicative of better executive functioning
LANGUAGE	Boston Naming Test (BNT)	Score from 0-15 representing the ability to name 15 items	Higher score is indicative of better cognitive domain functioning
EPISODIC MEMORY	Hopkin's Verbal Learning Test-Revised (HVLT-R)	Retention: % retained calculated by dividing the delayed recall trial by the higher of the 3 learning trials, with each trial scoring between 0-12.	Higher score is indicative of better cognitive domain functioning
ATTENTION	Digit Span Backwards (DSB)	Score from 0-16 representing the ability to repeat a number sequence read in the reverse order	Higher score is indicative of better cognitive domain functioning
GLOBAL COGNITION	Montreal Cognitive Assessment (MoCA)	Score from 0-30, sum of scores from subtests of cognitive function	A score of 26 implies absence of cognitive impairment

Table 3. Study population demographic, exposure, and outcome descriptions

Variable	**Mean (SD) or n (%)**
Age, years	64.03 (7.93)
Education, years	16.36(3.23)

Sex, female, n (%)	42(60.87%)
Ethnicity, African American, n (%)	27(39.13%)
Exposure – HeLIS (score)	5.58(1.55)
TMTB-A (s)	61.5(54.69)
DSB score (n)	6.84(27)
HVLT-R score (%)	46.71(10.4)
BNT score (n)	14(1.15)
MoCA score	25.45(3.79)

Table 4. Association of covariates with HeLIS

Covariate	β(95%CI)	p-value
Age	0.023(-0.02, 0.07)	0.3375
Gender(reference=Females)	0.63(-0.12, 1.38)	0.0993
Race(reference=African Americans)	1.01(0.29, 1.74)	0.007

Table 5. Unadjusted and adjusted regression analyses between HeLIS and cognitive outcomes

Cognitive Domain	**Test**	**Unadjusted**		**Adjusted for age, race, and gender**	
		β (95%CI)	P-value	β (95%CI)	P-value
Executive function	TMTB-A	**-10.08 (-18.34, -1.82)**	**0.0175**	**-10.14 (-18.57, -1.71)**	**0.0192**

Attention	Digit Span Backward	0.16 (-0.27, 0.58)	0.4652	0.233 (-0.23, 0.69)	0.3219
Episodic Memory	HVLT-R	1.28 (-0.33, 2.89)	0.1169	1.25 (-0.49, 3)	0.1565
Language	Boston Naming Test	**0.18 (0.002, 0.35)**	**0.0474**	0.18 (-0.003, 0.37)	0.0537
Global Cognition	MoCA	0.36(-0.23, 0.95)	0.2254	0.37(-0.23, 0.97)	0.2301

Table 6. Interaction assessment in adjusted models

Domain	Effect of Sex Males-Ref		Effect of Race Black- Reference	
	β*	P value	β*	P value
Executive function	-14.44	0.0743	15.66	0.0629
Episodic Memory	-1.72	0.308	-1.21	0.4926
Attention	0.08	0.8593	0.11	0.8214
Language	-0.18	0.3232	-0.25	0.1860
Global Cognition	0.15	0.7938	-0.82	0.1763

* Coefficient of the interaction term

Table 7a. Association of alcohol consumption levels with outcomes

Cognitive function	Level compared	Alcohol (reference='Poor')	
		β(95%CI)	P value
Executive function	Intermediate	19.02(-9.25, 47.29)	0.1838
	Ideal	46.61(-0.15, 93.37)	0.0507
Episodic memory	Intermediate	-2.09(-7.62, 3.43)	0.4518
	Ideal	-4.07(-13.2, 5.07)	0.3778
Language	Intermediate	-0.49(-1.09, 0.11)	0.1053
	Ideal	-0.72 (-1.71, 0.27)	0.1514
Attention	Intermediate	-0.95(-2.37, 0.48)	0.1889
	Ideal	-0.89(-3.24, 1.47)	0.4552
Global cognition	Intermediate	-2.05(-3.99, -0.11)	0.0386
	Ideal	-3.03 (-6.24, 0.17)	0.0632

Table 7b. Association of smoking status levels with outcomes

Cognitive function	Level compared	Smoking status (reference='Poor')	
		β(95%CI)	P value
Executive function	Ideal	**-58.9(-100.33, -17.46)**	**0.006**

Episodic memory	Ideal	**10.49(2.55, 18.43)**	**0.0104**
Language	Ideal	**1.27(0.4, 2.14)**	**0.0047**
Attention	Ideal	1.25(-0.89, 3.4)	0.2470
Global cognition	Ideal	2.09(-0.91, 5.09)	0.1689

Table 7c. Association of diet levels with outcomes

Cognitive function	Level compared	Diet (reference='Poor')	
		β(95%CI)	P value
Executive function	Ideal	-8.67(-43.53, 26.2)	0.6214
Episodic memory	Ideal	2.17(-4.45, 8.8)	0.5153
Language	Ideal	0	1
Attention	Ideal	-0.09(-1.82, 1.53)	0.9154
Global cognition	Ideal	1.65(-0.74, 4.04)	0.1718

Table 7d. Association of stress levels with outcomes

Cognitive function	Level compared	Stress (reference='Poor')	
		β(95%CI)	P value
Executive function	Intermediate	**-44.35(-77.56, -11.13)**	**0.01**
	Ideal	-40.6(-82.7, 1.52)	0.0586
Episodic memory	Intermediate	**7.89(1.57, 14.21)**	**0.0152**
	Ideal	3.01(-5.01, 11.03)	0.4559
Language	Intermediate	**0.81(0.10, 1.51)**	**0.0251**
	Ideal	**1.03(0.14, 1.91)**	**0.0246**
Attention	Intermediate	**1.74(0.07, 3.41)**	**0.0413**
	Ideal	1.54(-0.58, 3.66)	0.1521
Global cognition	Intermediate	1.54(-0.85, 3.92)	0.2025
	Ideal	2.26(-0.77, 5.28)	0.1409

Table 7e. Association of sleep levels with outcomes

Cognitive function	Level compared	Sleep (reference='Poor')	
		β(95%CI)	P value
Executive function	Intermediate	-4.91(-46.3, 36.48)	0.8136
	Ideal	-21.38(-60.44, 17.67)	0.2784

Episodic memory	Intermediate	6.89(-0.89, 14.65)	0.0816
	Ideal	6.74(-0.6, 14.07)	0.0711
Language	Intermediate	0.73(0.13, 1.59)	0.0954
	Ideal	0.68(-0.13, 1.49)	0.0983
Attention	Intermediate	0.13(-1.92, 2.18)	0.8957
	Ideal	0.95(-0.98, 2.88)	0.3292
Global cognition	Intermediate	2.27(-0.56, 5.09)	0.1145
	Ideal	**2.67(0.004, 5.341)**	**0.0497**

Table 7f. Association of physical activity levels with outcomes

Cognitive function	Level compared	Physical Activity (reference='Poor')	
		β(95%CI)	P value
Executive function	Intermediate	-19.18(-50.54, 12.19)	0.2267
	Ideal	**-37.35(-68.72, -5.98)**	**0.0204**
Episodic memory	Intermediate	3.96(-2.19, 10.1)	0.2029
	Ideal	2.09(-5.06, 8.23)	0.5
Language	Intermediate	0.30(-0.37, 0.98)	0.3728
	Ideal	0.48(-0.2, 1.16)	0.1632
Attention	Intermediate	-0.48(-2.09, 1.13)	0.5547
	Ideal	-0.13(-1.74, 1.48)	0.8719

Global cognition	Intermediate	-0.57(-2.82, 1.69)	0.6181
	Ideal	0.48(-1.78, 2.73)	0.6731