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Association of omega-3 levels and sleep in US adults, National Health and Nutrition Examination Survey, 2011-2012

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ABSTRACT

Objective: To determine associations between serum long-chain (LC) omega-3 fatty acid levels and sleep parameters among adults (N = 1314) in NHANES 2011-2012.
Methods: Regression analyses accounting for the complex-survey design were used to assess associations between serum LC omega-3 fatty acid levels, sleep duration, difficulty falling sleeping and sleep disorder.
Results: Overall, 48.6% were male, the mean age was 47.2 years, 5% reported very short sleep, 29% short sleep, 63% normal sleep and 3% long sleep. The sum of LC omega-3 fatty acid levels was lower among adults with short versus normal sleep, although differences were attenuated with adjustment for sociodemographic factors. Relative to normal sleep, adults with very short sleep had lower levels of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and sum of LC omega-3 fatty acids. Differences remained significant ($p < .05$ for all) with adjustment for sociodemographic factors. No associations were observed with difficulty falling sleeping or sleep disorder.
Conclusion: Our results suggest that omega-3 fatty acid levels are associated with healthy sleep duration, although, interventions are needed to clarify causality.

Introduction

The importance of healthy sleep, sleep length, and sleep quality is increasingly recognized as an important contributor to overall health.[1,2] However, 35% of adults in the United States report insufficient sleep (<7 hours duration).[3] As such, the Centers for Disease Control and World Health Organization have identified sleep deprivation as a major public health problem.[4] The prevalence of sleep disorders is growing, especially during the ongoing COVID-19 pandemic[5] necessitating new approaches to support sleep quality and duration.

Lifestyle behaviors, and in particular dietary intake, may be associated with sleep regulation via indirect and direct effects. Consumption of long-chain (LC) omega-3 polyunsaturated fatty acids (PUFAs) is part of a routine healthy dietary pattern[6] that support healthy weight and co-occurs with health promoting behaviors like physical activity and avoidance of alcohol that may improve sleep.[7] Preclinical studies have shown that EPA and DHA are important in regulating serotonin,[8] a modulator of both waking and sleep.[9] DHA is also involved in processes related to melatonin production.[10] Animals deficient in DHA have disturbed melatonin rhythm, dysregulated circadian clock function and greater sleep disturbances,[11] a finding that has been observed in children[12] who received total parenteral nutrition devoid of essential lipids.[13] Larger studies are however limited. Higher plasma DHA was associated with longer sleep duration among 405 Mexican adolescents[14] while oily fish intake was positively associated with sleep quality among 677 adults in Ecuador.[15] The aim of this study was therefore to examine cross-sectional associations between objective biomarkers of LC omega-3 fatty acid intake, with sleep duration, difficulty falling sleeping, and presence of a sleep disorder in a nationally representative sample of Americans.

Methods

Our study population was drawn from the National Health and Nutrition Examination Survey (NHANES) 2011-2012, the most recent year with data on circulating fatty acid levels, including omega-3 fatty acids. NHANES is designed to assess the nutritional status and

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Table 1
Associations between circulating LC omega-3 polyunsaturated fatty acids (%) and sleep duration among 1314 adults 19+ years

	Mean fatty acid levels, % (SE)							
	Very short	Short	Normal	Long	*P-v short*	*P-short*	*P-long*	
EPA	0.47 (0.04)	0.55 (0.04)	0.64 (0.03)	0.66 (0.12)	0.002*	0.07	0.89	
DPA	0.44 (0.01)	0.44 (0.01)	0.45 (0.01)	0.47 (0.02)	0.66	0.59	0.28	
DHA	1.09 (0.06)	1.32 (0.06)	1.42 (0.06)	1.53 (0.13)	<0.001*	0.08	0.39	
Sum LC omega-3	2.00 (0.09)	2.31 (0.10)	2.52 (0.08)	2.66 (0.26)	<0.001*	0.05	0.56	
	Model 1, ß (95% CI)				Model 2, ß (95% CI)			
	Very short	Short	Normal	Long	Very short	Short	Normal	Long
EPA	−0.18 (−0.28, −0.08)	−0.09 (−0.20, 0.01)	Ref	0.02 (−0.25,−0.28)	−0.11 (−0.21, −0.01)	−0.05 (−0.12, 0.03)	Ref	−0.04 (−0.28, 0.19)
DPA	−0.01 (−0.03, 0.02)	−0.01 (−0.03, 0.02)	Ref	0.02 (−0.02, 0.07)	0.01 (−0.01, 0.03)	−0.00 (−0.02, 0.02)	Ref	0.00 (−0.05, 0.06)
DHA	−0.33 (−0.44, −0.23)	−0.11 (−0.23, 0.01)	Ref	0.10 (−0.14, 0.34)	−0.26 (−0.40, −0.11)	−0.06 (−0.17, 0.05)	Ref	−0.00 (−0.25, 0.24)
Sum LC omega-3	−0.52 (−0.67, −0.37)	−0.21 (−0.41, −0.00)	Ref	0.14 (−0.36, 0.65)	−0.34 (−0.58, −0.11)	−0.10 (−0.28, 0.08)	Ref	−0.05 (−0.56, 0.47)

Means and *p* values reflect estimates and differences relative to normal sleep in unadjusted models (Model 1). Sample sizes are unweighted. However, estimates for means, proportions, standard errors (SE) were weighted using sampling weights for the fatty acids subsample. Very short (<5 hours), short (5-6 hours), normal (7-9 hours), and long (>9 hours) for those age <65 and very short (<5 hours), short (5-6 hours), normal (7-8 hours), and long (≥9 hours) for those aged 65+. Selection of confounders with backwards elimination resulted in adjustment for age, sex, race, PIR, and binge alcohol use for EPA, age, sex, race, binge alcohol use and BMI for DPA, age, sex, race, PIR, and binge alcohol use and BMI for DHA and the sum of LC omega-3 PUFA in model 2. Abbreviations: DPA; docosapentaenoic acid, DHA; docosahexaenoic acid, EPA; eicosapentaenoic acid, LC; long-chain

* Indicates $p < .05$ with adjustment for confounders in model 2.

health of Americans, using a complex multistage probability sampling design that is representative of the national civilian population in the United States.[16] This study was exempt from Institutional Review Board at the University of British Columbia related to the use of publicly available data for research and publication.

Fatty acid levels were measured in blood serum among a subsample of fasting participants aged 12 and older. Fatty acid levels were quantified using modified methods of Lagerstedt et al,[17] which included hexane extraction, and an internal standard solution of isotopically-labeled fatty acids to account for recovery. Fatty acids were resolved through injection on a capillary gas chromatograph column. Thirty-five fatty acids were measured, including the main exposures in this study: eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and DHA, and resultant total omega-3s. The lower limit of detection for EPA, DPA, and DHA were 0.79 μmol/L, 0.24 μmol/L, and 1.84 μmol/L, respectively. Fatty acids were expressed as a % of total fatty acids.

Sleep measures were assessed by an interviewer-administered computer-assisted personal interview in 6175 participants aged 16 and older. Sleep duration was determined from the question, "How much sleep do you usually get at night on weekdays or workdays?" Response categories ranged from 1 to 12 hours. Short sleep was categorized as very short (<5 hours) or short (5-6 hours).[18] Normal sleep and long sleep were defined as 7-9 hours and >9 hours for adults <65 years and as 7-8 hours, and >=9 hours for adults ≥65 years. Sleep quality was self-reported from 2 questions: "Have you ever told doctor or other health professional that you have trouble sleeping?" and "Have you ever been told by a doctor or other health professional that you have a sleep disorder?" Participant responses were yes, no, refused or don't know.

Study sample

Of the 6175 participants who completed sleep questionnaires, 2176 had serum fatty acids. Participants were excluded if they had missing data for any fatty acid (N = 2066) since fatty acids were expressed as a relative percent, were <19 years of age (N = 89), or were pregnant or breastfeeding (N = 21). This resulted in an analytical sample of 1314. Estimates for means, proportions, and standard errors (SE) were weighted using sampling weights for the fatty acid subsample. Sample sizes in the text and tables are unweighted. Variance estimates were determined using the Taylor Series Linearization approach. Differences between groups were determined by linear regression at $p < .05$ for the total analytical sample and stratified by sex and age groups that approximate life stages; younger adult (19-39), middle age (40-59) and older age (≥60). Model 1 was unadjusted. Model 2 was adjusted for confounders identified with backwards elimination until all variables in the model had a p-value less than 0.10. Potential confounders included age, gender, race/ethnicity (Non-Hispanic White, Hispanic/Mexican-American, Non-Hispanic Black, Asian and other/unknown), poverty to income ratio (PIR; low: 0-1.85, medium >1.85-3.50 and high: >3.50), education (<high school, high school and >high school), current smoking (yes/no), binge alcohol use (drinking≥4 drinks/d for women or ≥5 drinks/d for men on 12 or more occasions in a year), self-reported depression (yes/no) and BMI. As the confounders selected in a given model varied, confounders that met criteria are provided under Table 1. Statistical analyses were performed using survey procedures in STATA software version 14.2 (StataCorp, College Station, TX).

Results

Overall, 48.6% of the 1314 participants were male, the mean age was 47.2 years (SE = 0.81), 63.1% had college education or above, 19.2% were current smokers, 14.5% reported Mexican American or other Hispanic ethnicity, 67.6% non-Hispanic Whites, 11.7% non-Hispanic Black, 4.65% Asian and 1.47% reported other/unknown ethnicity. The majority (61.5%) were married or living with a partner, 47.4% had a high PIR, the mean BMI was 28.7 (SE = 0.33) and 13.6% reported use of an omega-3 supplement in the last 30 days (Supplemental Table 1).

Mean circulating LC omega-3 fatty acids and associations between LC omega-3 fatty acid levels and categories of sleep duration are shown in Table 1. Relative to normal sleep, adults with very short sleep had lower EPA, DHA and sum of LC omega-3 fatty acids. Differences remained significant when adjusted for covariates (ß = −0.11, 95% confidence interval [CI]: −0.21, −0.01 for EPA, ß = −0.26, 95% CI: −0.40, −0.11 for DHA and ß = −0.34, 95% CI: −0.58, −0.11 for sum LC omega-3). Compared to adults with normal sleep, adults with short sleep had marginally lower levels of EPA, DHA, and sum of LC omega-3. For example, ß = −0.321 95% CI: −0.41, 0.00 for sum of LC omega-3. When adjusted for covariates, differences were attenuated. No significant differences in LC omega-3 fatty acid levels were observed between normal and long sleep. Differences between omega-3 fatty acid levels and sleep duration stratified by sex and age groups are provided in Supplemental Tables 2 and 3, and generally followed similar patterns as in the overall population.

Table 2
Associations between circulating LC omega-3 polyunsaturated fatty acids (%) and sleep duration among 1314 adults 19+ years

	Difficulty falling asleep			
	Mean fatty acid levels, % (SE)		*p*	
	No	Yes		
EPA	0.62 (0.03)	0.57 (0.04)	.42	
DPA	0.45 (0.01)	0.44 (0.01)	.62	
DHA	1.40 (0.05)	1.30 (0.08)	.14	
Sum LC omega-3	2.47 (0.08)	2.31 (0.14)	.25	
	Model 1, ß (95% CI)		Model 2, ß (95% CI)	
	No	Yes	No	Yes
EPA	Ref	0.50 (−0.08 0.18)	Ref	0.08 (−0.03, 0.18)
DPA	Ref	0.01 (−0.03, 0.04)	Ref	0.01 (−0.02, 0.04)
DHA	Ref	0.10 (−0.04, 0.25)	Ref	0.06 (−0.04, 0.16)
Sum LC omega-3	Ref	0.16 (−0.12, 0.45)	Ref	0.13 (−0.08, 0.34)
	Presence of sleep disorder			
	Mean fatty acid levels, % (SE)		*p*	
	No	Yes		
EPA	0.60 (0.55, 0.66)	0.65 (0.49, 0.82)	.42	
DPA	0.45 (0.44, 0.46)	0.46 (0.42, 0.50)	.62	
DHA	1.38 (1.27, 1.50)	1.33 (1.18, 1.49)	.14	
Sum LC omega-3	2.43 (2.27, 2.59)	2.44 (2.11, 2.77)	.25	
	Model 1, ß (95% CI)		Model 2, ß (95% CI)	
	No	Yes	No	Yes
EPA	Ref	−0.05 (−0.22, 0.12)	Ref	0.00 (−0.17, 0.18)
DPA	Ref	−0.01 (−0.05, 0.03)	Ref	−0.01 (−0.04, 0.04)
DHA	Ref	0.05 (−0.08, 0.19)	Ref	0.04 (−0.11, 0.18)
Sum LC omega-3	Ref	−0.01 (−0.32, 0.30)	Ref	0.02 (−0.32, 0.36)

p values reflect differences relative to normal sleep in unadjusted models (Model 1). Abbreviations: DHA; docosahexaenoic acid, DPA; docosapentaenoic acid, EPA; eicosapentaenoic acid, LC; long-chain

Overall, 24.4% reported having difficulty falling sleeping while 8.67% reported having a sleep disorder. Levels of EPA, DPA, DHA, and the sum of LC omega-3 fatty acids were similar between adults with and without difficulty falling sleeping and with and without a sleep disorder (Table 2).

Discussion

This study adds to evidence on the importance of LC omega-3 fatty acids for overall health and wellness, including sleep, by providing novel data on biomarkers of omega-3 intake in a large, nationally representative population of Americans. Our findings showed that levels of EPA, DHA, and the sum of omega-3 fatty acids were persistently lower among those with very short sleep relative to normal sleep. The lack of differences in omega-3 fatty acid levels between normal versus long sleep duration and difficulty falling sleeping may suggest a null effect of LC omega-3 fatty acids on sleep consolidation/quality. This is supported by a recent randomized clinical trial of supplementation with either DHA, EPA or placebo on sleep, that reported indices of sleep quality (awakenings and sleep fragmentation index) were similar between all 3 groups.[19] There was no benefit of EPA and DHA supplementation on sleep duration, although a trend towards increased sleep efficiency in the EPA group versus placebo was observed, suggesting, similar to our results, benefits of EPA on a healthy sleep cycle.

It is possible the relationships observed between sleep duration and circulating levels of omega-3 fatty acids reflects that omega-3 levels are a marker of sociodemographic factors. For example, lower omega-3 intake has been observed among adults with lower educational attainment, lower income, and less access to high quality nutrient dense food.[20] Or, relationships may reflect lifestyle factors since lower omega-3 intake has been observed among adults with higher BMI.[21]

Strengths of this study include use of serum concentrations of LC omega-3s, which reflects both diet and metabolism and are not influenced by bias and error of self-reported dietary intake and use of data from a US nationally representative population. However, few reported very short and long sleep duration, and the prevalence of sleep disorder was low, which may have reduced our power to detect differences. Dietary intake of omega-3 fatty acids are persistently low in the United States[22,23] and it is possible the levels of omega-3 fatty acids were too low and/or the range was too limited to detect modest relationships. The cross-sectional nature of NHANES precludes the ability to determine causal relationships. Further limitations include the self-reported nature of sleep parameters and lack of information on sleep duration on the weekends which may introduce systematic bias and obscure true associations.

Although additional research is needed to clarify causality and underlying mechanisms, our results suggest efforts to increase regular intake of dietary omega-3 fatty acids could improve sleep. Future innovation in omega-3 diagnostics may lead to more widespread measurement of an individual's omega-3 fatty acid status that will allow for personalized dietary recommendations. Continued efforts to raise public health awareness and educate healthcare practitioners on the wide ranging health benefits of omega-3 fatty acids continue to be needed.

Data statement

Data are available in a public, open access repository. The dataset used for this study was generated from publicly available data from the National Health and Nutrition Examination Survey (NHANES).

Conflict of Interest

RAM carried out the work presented in the manuscript as a consultant for Pharmavite. PPD, SE, KM, and SHM are employees of Pharmavite, LLC, manufacturers and suppliers of omega-3 nutritional lipids.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.sleh.2021.12.003.

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