Original research paper

Assessment of dietary adequacy for important brain micronutrients in patients presenting to a traumatic brain injury clinic for evaluation

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Objective: To evaluate dietary adequacy of patients presenting for evaluation at an outpatient traumatic brain injury (TBI) clinic.
Methods: We identified 14 key micronutrients with defined dietary intake reference ranges that are considered important for brain health. Adult patients completed the Brief NutritionQuest Food Frequency Questionnaire (FFQ) to calculate estimated nutrient intake. Medical records were abstracted for diagnoses, body mass index, and neurobehavioral subscale scores. Nutrients were assessed individually and were also summarized into a summary score. Associations between individual nutrients, summary nutrient intake, and neurobehavioral scores were assessed.
Results: A total of 39 FFQs were completed by subjects, and 25 (64%) had recorded neurobehavioral scores. No subjects met the recommended dietary allowances (RDAs) for all 14 micronutrients. Ten (26%) met the RDAs for 6 or fewer nutrients, and 10 met the RDAs for 11–12 nutrients. Of 12 nutrients with sufficient sample size for analysis, 11 (92%) were associated with worse mean somatic scores, 9 (75%) were associated with worse cognitive scores, and 8 (67%) were linked with worse affective scores for those with the lowest nutrient intake compared with those who had the highest intake. However, only four nutrients were statistically associated with the somatic mean score: folate ($P = 0.010$), magnesium ($P = 0.082$), vitamin C ($P = 0.021$), and vitamin K ($P = 0.024$). None were linked with cognitive or affective scores.
Discussion: Diets failing to meet RDAs for important brain nutrients were common in an outpatient TBI clinic, with the worst mean neurobehavioral scores for those patients not meeting the estimated average requirements.

Keywords: Traumatic brain injury, Nutrition, Recovery, Diet, Vitamins, Minerals, Essential fatty acids

Introduction

Supportive nutrition is considered a critical part of treating patients with acute severe traumatic brain injury (TBI), but there is little research on the role of nutrition in milder forms of TBI that do not require hospitalization, and there is no specific standard of nutritional care for TBI patients after discharge from the hospital. TBI is a major public health concern; as many as 1.7 million Americans suffer TBIs every year, and an estimated 235 000 are hospitalized. The leading causes of TBI related to deaths, hospitalizations, and emergency department visits are falls (28%), motor vehicle accidents (19%), and assaults (11%). An estimated 43% of those who suffer TBI will develop a long-term disability as a result. Although approximately 75% of all TBIs presenting to the emergency room are classified as mild, 5–20% of these will develop chronic post-concussive somatic or neurobehavioral symptoms.[1]

The past decade of military conflicts in Afghanistan and Iraq are notable in that TBI is considered a signature injury. Data from the US Armed Forces Health Surveillance Center indicate that 262 065 TBIs were sustained by military personnel between 2000 and the third quarter of 2012.[2] In response to this high rate of TBI and to better understand the lasting sequelae that follow, the Departments of Defense and

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Veteran Affairs have created comprehensive programs for evaluating and treating veterans who experienced TBI and residual symptoms.

A multidisciplinary team approach has been adopted within the Veteran Affairs Health Administration VA, and a significant amount of funds have been allocated for TBI research, with a key goal of improving interventions. One emerging area of focus, in both clinical and research settings, is the role of nutrition.

Lewis and Bailes advised that the military administer omega-3 fatty acids to protect soldiers at risk for TBI in the line of duty.[2,3] However, their research does not provide any specific nutritional recommendations for those who have already received mild or moderate TBI. Although large numbers of soldiers are returning from the current wars with a history of exposures to blast and other potential causes of TBI, there are little data on diet quality or the correlation between diet and the severity of neurobehavioral (physical, cognitive, and affective) symptoms reported by the patients.

The aims of this study were four-fold. The first was to identify data from a veteran sample on the consumption of vitamins, minerals, essential fatty acids, and antioxidants reported to be important for optimal brain function. The second was to assess the adequacy of the diet in patients presenting for an evaluation of possible TBI in providing those nutrients. Third, we wanted to assess the relationship between micronutrient intake and neurobehavioral symptom burden. The fourth was to measure the effect size required to collect pilot data for a grant that would be sufficiently powered to detect differences and would have recruitment targets to ensure appropriate representation of women and minorities in the study. Our hypotheses were (1) that many of the patients presenting for evaluation for possible TBI are consuming diets that are not meeting the recommended dietary allowances (RDAs) for micronutrients considered helpful for optimal brain physiology, and (2) the micronutrient intakes are correlated with neurobehavioral symptom severity.

Methods

The University of Iowa and the Iowa City VA Institutional Review Board approved the research plan and these analyses. Using the criteria described by Bourre[4,5] regarding macronutrient and micronutrient intake and the brain, we identified micronutrients important to optimal brain function, 14 of which have established dietary reference intake (DRI) ranges. We focused on measuring the estimated nutrient intake of nutrients with DRIs. The study setting was a Veterans Affairs Medical Center Level III Polytrauma Clinic affiliated with a university in the Midwest. The subjects were adult outpatients who were referred for evaluation of possible TBI based on self-reported exposure during military service with immediate and lasting sequelae. Consecutive adult patients referred to the Polytrauma Clinic were invited to participate in the study between 11 March 2009 and 20 December 2011. All subjects had a history of a documented TBI; blast injury; or a head injury involving a fall, bullet wound, vehicular accident, or other type of head injury and subsequent, ongoing neurobehavioral symptoms. A medically confirmed TBI was not an inclusion criterion. The exclusion criteria were incompetence or age younger than 18 years.

Patients completed the NutritionQuest Brief 2000 Food Frequency Questionnaire (FFQ),[6] and the results were used to generate estimated nutrient intake for each respondent. Due to resource constraints, we were unable to interview the subjects to collect information about their food intake and use of energy drinks and supplements during their military service, but we plan to do so in follow-up studies related to nutrition and TBI among veteran patients. Cut-off nutrient values were based on age- and gender-specific estimated average requirements (EARs) and the RDAs in the DRIs from the Food and Nutrition Board.[7] EAR is considered the micronutrient intake that would meet the needs for half of the population, while RDA is the intake level that would meet the needs of ~98% of the population. Medical records were abstracted for responses to the neurobehavioral symptoms checklist (for checklist, see Appendix), body mass index (BMI), demographics, diagnoses, and prescription medications. The standardized VA assessment of TBI includes completion of the 21 Neurobehavioral Checklist[8] as part of a broader evaluation. BMI classifications were taken from the World Health Organization categories.[9] No other behavior or mood assessments were carried out. We did not assess any laboratory tests as part of the study.

Variable creation

Age was divided into two groups: 22–29 years and 32–47 years. BMI was divided into three groups: <25 (normal), 25–29.9 (overweight), and >30 (obese). The numbers of comorbidities and medical and psychological problems (range 1–15) were classified into three groups: 1–3, 4–5, and 6–15. Medications were classified into three groups: 0–1, 2–3, and ≥4. The Neurobehavioral Instrument questions were summed to form a total score and subscores for affective, somatic, and cognitive areas.[8] These four scores were also classified into categories to form ordinal variables and for comparison with continuous variables. The 14 nutrient variables were classified in

various ways. A three-group variable (labeled 1, 2, or 3) for each nutrient was also created, with 1 representing ≤EAR, 2 ≥EAR to <RDA, and 3 ≥RDA. We also created a single summary score by adding the 14 three-group nutrients with a potential range from 14 to 52. The summary score was tested for reliability using Cronbach's alpha coefficient of internal consistency, and the results indicated very good reliability ($\alpha = 0.88$).

Statistical methods

Because of small samples sizes, unadjusted associations among categorical variables were assessed using Fisher's exact tests. The Cochran–Armitage trend test was used to assess the hypothesis that more symptomatic scores were associated with poorer nutritional intake. Associations between continuous nutrient values or neurobehavioral scores and categorical demographic or clinical characteristics were evaluated by comparing unadjusted mean differences (standard errors, SE) by the categories. Means and *P* values (using *t*-tests for two means) were generated with general linear model methods. Two-sided statistical significance was set at $\alpha \leq 0.10$, and all analyses were performed with SAS 9.2, SAS Institute Inc., Cary, NC, USA, 2002–2010.

Results

Demographic and clinical characteristics

Demographic and clinical characteristics were obtained for all 39 patients with nutrient intake values, and data from the 25 patients with neurobehavioral scores are displayed in Table 1. Because patients without neurobehavioral data were seen prior to the introduction of that measure within the VA, statistical differences between those with complete data and missing data were most likely due to non-systematic variance from the small sample sizes. The 39 patients included 35 men and 4 women with ages ranging from 22 to 54 years and a mean age of 33.6 years (SE: 1.4). The mean age of the 25 patients was younger than the full sample (31.7 years, SE: 1.6). Most participants were white, and one was Hispanic (data not shown). Twenty-eight (72%) patients were current smokers, and 78% reported previously drinking more than the amount they currently consumed. Patients were taking an average of 3.7 medications, with the number of medications ranging from none to 17. There was no significant difference in gender for BMI, greater alcohol consumption, current smoking, or number of medications prescribed. Approximately 31% of the patients reported five or fewer comorbid conditions, while 69% reported six or more conditions. There were no significant differences by categorical comorbidity (grouped by numbers) between the proportion of patients in the nutrient intake group and the smaller neurobehavioral group. However, there was a significant difference in the number of mean comorbidities ($P = 0.008$), with the complete nutrient intake group reporting 6.8 (SE: 0.6) conditions compared to 5.6 (SE: 0.6) in the smaller group.

Table 1 Demographic characteristics

Characteristics	Complete nutrient intake* (*N* = 39)	Complete neurobehavioral scores (*N* = 25)	*P* value** (*N* = 14)
Mean (SE) age in years	33.6 (1.4)	31.7 (1.6)	0.073
Range	22–54	22–47	
Age in years			0.043
22–29	18 (46.2)	15 (60.0)	
32–47	21 (53.8)	10 (40.0)	
Gender			0.609
Male	35 (89.7)	23 (92.0)	
Female	4 (10.3)	2 (8.0)	
BMI***			0.606
Normal	7 (18.9)	5 (21.7)	
Overweight	16 (43.2)	11 (47.8)	
Obese	14 (37.8)	7 (30.4)	
Ever drank more			0.682
Yes	28 (77.8)	17 (73.9)	
No	8 (22.2)	6 (26.1)	
Current smoker			0.713
Yes	28 (71.8)	17 (68.0)	
No	11 (28.2)	8 (32.0)	
Mean (SE) comorbidities	6.8 (0.6)	5.6 (0.6)	0.008
Range	1–17	1–15	
Comorbidities (number)			0.302
1–3	7 (17.9)	6 (24.0)	
4–5	5 (12.8)	4 (16.0)	
6–17	27 (69.2)	15 (60.0)	
Mean (SE) medications	3.7 (0.5)	3.1 (0.4)	0.211
Range	0–17	0–8	
Medications (number)			0.837
0–1	12 (30.8)	8 (32.0)	
2–3	10 (25.6)	7 (28.0)	
≥4	17 (43.6)	10 (40.0)	
Nutrient intake groups			0.025
Low	13 (33.3)	11 (44.0)	
Middle	12 (30.8)	9 (36.0)	
High	14 (35.9)	5 (20.0)	

*Values listed are *N* (%) except where noted as mean (SE).
***P* value generated from Fisher's exact test for small sample sizes – difference between patients with complete and missing data.
***BMI = weight/height^2: Normal = 19.0–24.99, Overweight = 25–29.99, Obese ≥ 30.0.

Food frequency questionnaire(s)

Thirty-nine patients completed the FFQ. No patient met the RDAs for all 14 nutrients (Table 2). Ten patients (26%) fulfilled the requirements for 11 or more nutrients, while 10 patients fulfilled 6 or fewer requirements. Everyone met the RDA criterion for

Table 2 Rank order of intake nutrients by adherence to EAR and RDA standards

Rank	Below EAR		≥EAR–< RDA		≥RDA	
	Nutrient	*N* (%)	Nutrient	*N* (%)	Nutrient	*N* (%)
14	Vitamin D	0 (0.0)	Vitamin D	0 (0.0)	Vitamin D	39 (100.0)
13	Iron	3 (7.7)	Vitamin K	0 (0.0)	Vitamin B12	35 (89.7)
12	Vitamin B6	3 (7.7)	Vitamin B12	0 (0.0)	Vitamin B6	33 (84.6)
11	Thiamine	4 (10.3)	Vitamin B2 (Riboflavin)	2 (5.1)	Vitamin B2 (Riboflavin)	32 (82.1)
10	Vitamin B12	4 (10.3)	Vitamin C	2 (5.1)	Iron	31 (79.5)
9	Niacin	5 (12.8)	Vitamin B6	3 (7.7)	Thiamine	31 (79.5)
8	Vitamin B2 (Riboflavin)	5 (12.8)	Vitamin E	3 (7.7)	Niacin	28 (71.8)
7	Vitamin C	12 (30.8)	Thiamine	4 (10.3)	Vitamin C	25 (64.1)
6	Zinc	13 (33.3)	Iron	5 (12.8)	Vitamin K	23 (59.0)
5	Vitamin K	16 (41.0)	Vitamin A	5 (12.8)	Zinc	19 (48.7)
4	Folate	20 (51.3)	Niacin	6 (15.4)	Folate	13 (33.3)
3	Magnesium	26 (66.7)	Folate	6 (15.4)	Magnesium	4 (10.3)
2	Vitamin E	33 (84.6)	Zinc	7 (17.9)	Vitamin E	3 (7.7)
1	Vitamin A	34 (87.2)	Magnesium	9 (23.1)	Vitamin A	0 (0.0)

*EAR, estimated average requirements; RDA, recommended dietary allowance.

vitamin D, but no patient met the RDA criterion for vitamin A. The other RDA nutrient recommendations that patients met the most frequently were B12 ($n = 35$, 90%), B6 ($n = 33$, 85%), and iron and thiamine ($n = 31$, 80%). The RDA recommendations that were met the least frequently were manganese ($n = 4$, 10%) and vitamin E ($n = 3$, 8%). There was a significant difference in the distribution within the nutrient intake group based on summary nutrient score ($P = 0.025$) between the 39 patients and the 25 patients (Table 1). In the larger group, the proportions for low, middle, and high intakes were 33, 31, and 36%, respectively. In the neurobehavioral group, the proportion in the highest group dropped to 20% and increased to 36 and 44% in the middle and lowest groups, respectively.

Neurobehavioral questionnaire

Higher neurobehavioral scores indicate more severe symptom burden. The total scores ranged from 10 to 75; 3 to 32 for the somatic score, 0 to 16 for the cognitive score, and 4 to 27 for the affective score. None of the neurobehavioral scores were associated with age, gender, BMI, drinking, or smoking (data not shown). The number of comorbid conditions and medications was associated with the affective score. Patients with 1 to 3 conditions had the lowest mean score (9.7, SE: 2.0), and were significantly different from those with 6 or more conditions and a mean score of 16.1 (SE: 1.2) ($P = 0.024$, data not shown). Patients with 4 or 5 conditions had a mean of 12.3 (SE: 2.0). Medications followed a similar pattern ($P = 0.046$, data not shown), with the lowest mean score among those taking the fewest medications (0–1 medications, mean = 11.3, SE: 1.7) and the highest mean score among those taking 5 or more medications (mean = 17.5, SE: 1.5).

Of the 12 nutrients with sufficient sample size for analysis (Table 3), 11 (92%) displayed worse mean somatic scores (difference ≥2.4), 9 (75%) displayed worse cognitive scores (difference ≥1.0), and 8 (67%) displayed worse affective scores (difference ≥1.1) for those with the lowest nutrient intake compared with those with higher intake. However, only four nutrients were statistically associated with the somatic mean score (range in differences 7.7–9.9 points), and none were linked with the cognitive or affective scores: folate ($P = 0.010$), manganese ($P = 0.082$), vitamin C ($P = 0.021$), and vitamin K ($P = 0.024$). The next largest, but non-significant, somatic mean differences were for thiamine (5.9 points) and vitamin B12 (7.0 points).

Table 4 displays the results for neurobehavioral scores by the summary nutrient intake groups. Only the somatic mean scores for the low- and high-nutrient groups showed a significant difference, with means of 16.9 vs. 7.0, respectively ($P = 0.038$). The categorical somatic, cognitive, and affective scores (four groups) displayed similar patterns for the low- and high-intake groups. Between 55 and 64% of the low-intake group were in the two worst (most symptomatic) categories, whereas 80% of the high-intake group was in the best (least symptomatic) category. However, only the somatic score showed a statistically significant association ($P = 0.017$). Within the four somatic categories, around 64% the low-intake group had a score of 12 or greater, while 80% of the high-intake group had a score below 6 (mild symptoms).

Results: power and sample size

This analysis allowed us to determine power and sample sizes for future studies. With a larger sample size, many of the differences found in this study would reach statistical significance ($P < 0.05$). For the somatic score, a minimum mean difference of 5.0–5.5 points would be detected with 40–45 patients for those with a nutrient intake <EAR vs. ≥RDA at 85% power and $\alpha = 0.05$. For the cognitive score,

Table 3 Neurobehavioral mean (SE) score by nutritional intake standards

Nutrient groups	Total score Mean (SE)	Somatic Mean (SE)	Cognitive Mean (SE)	Affective Mean (SE)
Folate_				
< EAR	41.8 (4.0)	16.9 (1.9)	9.1 (1.0)	15.7 (1.4)
EAR– <RDA	21.3 (9.2)	4.7 (4.3)	4.7 (2.4)	12.0 (3.2)
≥ RDA	27.3 (6.5)	7.3 (3.1)	8.0 (1.7)	12.0 (2.2)
P value	*0.059*	*0.010*	*0.252*	*0,294*
Iron				
< EAR	27.5 (12.3)	10.0 (6.1)	6.0 (3.1)	11.5 (4.0)
EAR– <RDA	46.3 (10.1)	21.3 (5.0)	8.0 (2.5)	17.0 (3.3)
≥ RDA	35.1 (3.9)	12.3 (1.9)	8.6 (1.0)	14.3 (1.3)
P value	*0.466*	*0.228*	*0.722*	*0.566*
Manganese				
< EAR	38.2 (3.8)	14.7 (1.9)	8.6 (1.0)	14.9 (1.2)
EAR– <RDA	26.4 (7.6)	7.0 (3.8)	7.2 (1.9)	12.2 (2.5)
≥ RDA	NA	NA	NA	NA
P value	*0.177*	*0.082*	*0.522*	*0.343*
Niacin				
< EAR	40.7 (10.2)	16.7 (5.2)	9.3 (2.5)	14.7 (3.3)
– <RDA	41.6 (7.9)	15.2 (4.0)	9.8 (1.9)	16.6 (2.5)
≥RDA	33.3 (4.3)	11.9 (2.2)	7.7 (1.1)	13.6 (1.4)
P value	*0.580*	*0.610*	*0.588*	*0.598*
Thiamine				
< EAR	42.3 (8.9)	18.3 (4.5)	8.3 (2.1)	15.8 (2.9)
EAR– < RDA	35.5 (12.6)	10.5 (6.3)	12.0 (3.0)	13.0 (4.1)
≥RDA	34.5 (4.1)	12.4 (2.0)	7.9 (1.0)	14.2 (1.3)
P value	*0.736*	*0.457*	*0.458*	*0.838*
Vitamin A				
<EAR	34.2 (3.2)	12.4 (1.7)	8.0 (0.8)	13.8 (1.0)
EAR– < RDA	NE	NE	NE	NE
≥RDA	NE	NE	NE	NE
P value				
Vitamin B2 riboflavin				
<EAR	41.6 (7.9)	17.0 (4.0)	9.0 (1.9)	15.6 (2.6)
EAR– < RDA	39.0 (17.8)	14.0 (9.0)	12.0 (4.3)	13.0 (5.8)
≥RDA	34.2 (4.1)	12.1 (2.1)	7.9 (1.0)	14.1 (1.3)
P value	*0.699*	*0.564*	*0.619*	*0.852*
Vitamin B6				
<EAR	40.7 (10.4)	16.7 (5.2)	9.3 (2.4)	14.7 (3.4)
EAR– < RDA	36.0 (12.7)	17.0 (6.4)	4.0 (3.0)	15.0 (4.1)
≥RDA	35.1 (4.0)	12.3 (2.0)	8.6 (0.9)	14.3 (1.3)
P value	*0.883*	*0.610*	*0.362*	*0.980*
Vitamin B12				
<EAR	43.3 (10.1)	19.3 (5.0)	8.0 (2.5)	16.0 (3.3)
EAR– < RDA	NA	NA	NA	NA
≥RDA	34.8 (3.7)	12.3 (1.9)	8.4 (0.9)	14.1 (1.2)
P value	*0.435*	*0.205*	*0.893*	*0.597*
Vitamin C				
<EAR	45.3 (5.0)	18.7 (2.5)	9.6 (1.4)	17.0 (1.7)
EAR– < RDA	36.0 (11.3)	14.0 (5.5)	8.0 (3.0)	14.0 (3.8)
≥RDA	28.5 (4.4)	8.8 (2.2)	7.4 (1.2)	12.4 (1.5)
P value	*0.064*	*0.021*	*0.480*	*0.143*
Vitamin E				
<EAR	36.4 (3.7)	13.5 (1.9)	8.3 (0.9)	14.6 (1.2)
EAR– < RDA	NA	NA	NA	NA
≥RDA	29.5 (12.4)	9.0 (6.3)	9.0 (3.1)	11.5 (4.0)
P value	*0.599*	*0.501*	*0.819*	*0.461*
Vitamin K				
<EAR	41.5 (4.6)	16.9 (2.2)	8.8 (1.2)	15.8 (1.5)
EAR– < RDA	NA	NA	NA	NA
≥RDA	29.7 (4.8)	9.1 (2.3)	7.8 (1.2)	12.8 (1.6)
P value	*0.086*	*0.024*	*0.531*	*0.194*
Zinc				
<EAR	39.6 (5.3)	15.4 (2.7)	8.6 (1.3)	15.6 (1.7)
EAR– < RDA	35.7 (7.2)	11.5 (3.7)	9.3 (1.8)	14.8 (2.3)
≥RDA	30.8 (6.2)	11.4 (3.2)	7.1 (1.5)	12.3 (2.0)
P value	*0.562*	*0.565*	*0.616*	*0.430*

EAR, estimated average requirements; RDA, recommended dietary allowance.

Table 4 Comparison of neurobehavioral scores by nutritional intake groups

	Nutritional score groups			Mean comparisons		
Neurobehavioral mean scores	Low Mean (SE)	Middle Mean (SE)	High Mean (SE)	High vs. low *P* value*	High vs. middle *P* value*	Middle vs. low *P* value*
Total score	40.9 (5.4)	34.9 (5.8)	26.4 (6.5)	0.130	0.383	0.442
Range	16–69	10–75	18–52			
Somatic	16.9 (2.6)	12.0 (2.9)	7.0 (3.0)	0.038	0.294	0.204
Range	5–30	3–32	4–19			
Cognitive score	8.7 (1.4)	8.4 (1.5)	7.2 (1.2)	0.526	0.616	0.888
Range	3–16	0–16	5–12			
Affect score	15.3 (1.7)	14.4 (2.1)	12.2 (2.3)	0.327	0.487	0.749
Range	7–25	4–27	9–21			
Neurobehavioral score groups	Nutritional score groups			Trend tests		
	Low *N* (%)	Middle *N* (%)	High *N* (%)	High vs. Low *P* value**	High vs. Middle *P* value**	Middle vs. Low *P* value**
Total score				0.106	0.327	0.254
10–20	2 (18.2)	1 (11.1)	3 (60.0)			
21–34	2 (18.2)	4 (44.4)	1 (20.0)			
35–39	2 (18.2)	3 (33.3)	0 (0.0)			
47–75	5 (45.5)	1 (11.1)	1 (20.0)			
Somatic score				0.017	0.206	0.094
3–5	1 (9.1)	2 (22.2)	4 (80.0)			
6–11	3 (27.3)	3 (33.3)	0 (0.0)			
12–21	3 (27.3)	3 (33.3)	1 (20.0)			
23–32	4 (36.4)	1 (11.1)	0 (0.0)			
Cognitive score				0.686	0.695	0.454
0–5	4 (36.4)	2 (22.2)	1 (20.0)			
6–7	1 (9.1)	2 (22.2)	3 (60.0)			
8–11	3 (27.3)	2 (22.2)	0 (0.0)			
12–16	3 (27.3)	3 (33.3)	1 (20.0)			
Affect score				0.123	0.747	0.592
4–10	2 (18.2)	1 (11.1)	3 (60.0)			
11–13	2 (18.2)	3 (33.3)	1 (20.0)			
14–17	3 (27.3)	3 (33.3)	0 (0.0)			
18–27	4 (36.4)	2 (22.2)	1 (20.0)			

*P value generated from a T-test for 2 means.
**P value generated from the Cochran–Armitage trend test.

minimum mean significant differences would be detected for 3.0–3.5 points with 45–50 patients per group. For the affective score, the point difference would be 4.0–5.5 with 40–50 patients.

Discussion

Many patients in this study who presented for evaluation for possible TBI consistently consumed diets that were lacking in multiple micronutrients considered important for optimal brain health. Patients with the lowest overall nutrient intake displayed the worst mean neurobehavioral scores, although the only significant association was with the somatic score. Worse mean neurobehavioral scores were also observed across the majority of individual nutrients for patients consuming less than the EAR standard, even though only the somatic score showed significant associations with folate, magnesium, vitamin C, and vitamin K. Patients with worse neurobehavioral mean scores were also taking more medications and had more comorbidities (only the affective score displayed statistically significant associations). This finding is of concern because individuals who reported the highest level of somatic complaints were consuming less than adequate diets.

The important relationship between diet nutrient density and health status is well known. Our findings are consistent with the observation that the diets of many Americans fail to meet the RDAs for multiple water- and fat-soluble vitamins and minerals.[10] Furthermore, they are consistent with the observation that patients with mood disorders are more likely to have B vitamin-deficient diets.[11]

Because the diets of so many Americans fail to meet the RDAs for multiple micronutrients, tools have been developed to improve the consumption of nutrient-dense foods. Using a healthy eating index score to assess the diets of outpatients and guide food selection would likely benefit patients recovering from TBI, but nutrition counselling to increase diet nutrient density is not currently part of the standard of care for outpatient treatment of TBI.

Our study increases the understanding of the nutritional status of TBI outpatients and highlights the importance of holistic intervention. The vast majority of studies on TBI and nutrition are focused on acute severe brain injury; few assess the nutritional aspects

of central nervous system injury in an outpatient setting. Multiple studies of the diets of spinal cord-injured patients have revealed that patients often fail to meet the RDAs for multiple vitamins, minerals, and essential fatty acids.[12–15] In an open-label pilot study of former National Football League (NFL) football players suffering from the effects of TBI, a nutritional intervention comprised high-potency B vitamins, omega-3 fatty acids, antioxidants (*N*-acetyl-cysteine and lipoic acid), acetyl-l-carnitine, gingko, vinpocetine, and huperzine improved cognition and cerebral blood flow.[16] We could not find any other studies on TBI outpatient nutritional status.

Several authors have discussed the nutritional needs of the brain at both macro- and micro-levels,[4,5,17] stressing the need for nutrient-dense diets that supply ample levels of vitamins, minerals, antioxidants, and essential fatty acids. Additionally, methyltetrahydrofolate, methyl cobalamin, and methylation pathways are critically important at the mitochondrial level,[18,19] and will therefore have a major impact on brain tissue recovery and function. That we observed the strongest correlations between vitamin B12 and folate intake levels and symptoms is consistent with these nutrients' important roles in bioenergetics and brain metabolism.

Although multiple authors have written about the nutritional requirements of the human brain, no study has prospectively defined the optimal nutrients or their optimal recommended doses. Although RDA and EAR values have been established, levels of nutrient intake for optimal health have not. In analysis of the diets of hunter-gatherer societies, the intake of vitamins, minerals, and essential fatty acids exceeded RDAs by factors of 2 to 10 depending on the nutrient (10). The diets of free-living primates, our closest animal relatives, have also been analyzed, and their intake of vitamins and antioxidants far exceeded the RDAs for human nutrition.[20] An intervention designed to provide intensive nutritional support of mitochondria and neurons using B vitamins and antioxidants to treat neurodegenerative disease has been advocated by Kidd[19] and was utilized in part in a study of former NFL players suffering from the effects of cumulative TBIs. The use of diet and a targeted supplement program specifically designed to maximize the intake of micronutrients identified as important to the brain and mitochondria physiology may offer significant benefits with minimal risk of adverse events.

In addition, the microbiome, that is, the mix of bacteria, yeasts, and parasites living in the gut, is increasingly recognized to have a major impact on mood and behavior.[21] Diet and lifestyle strongly influence which microbial species predominate in the microbiome,[22] with the intake of highly processed carbohydrates increasing the probability of a microbiome associated with higher risk of mental health problems.[21]

Nutrient intake as measured by FFQs is an imprecise measure because of both recall bias and individual variation in nutrient absorption. As such, it would be preferable to assess actual levels of nutrient biomarkers and their relationship to brain function. One study of a geriatric population examined nutrient biomarkers, cognitive assessments, and brain volume measured by magnetic resonance imaging. Bowman *et al.*[23] documented the associations between blood biomarker levels of vitamins, minerals, essential fatty acids, and antioxidants and cognition and brain volume, adding more support to the hypothesis that a nutrient-dense diet could help patients recovering from TBI.

Kidd advocates the use of intensive nutritional support using B vitamins, essential fatty acids, and a variety of antioxidants to improve mitochondrial function and treat neurodegeneration[19] many of which would be provided by consuming a nutrient-dense diet. We relied on the studies by Bourre[4,5,24] and Bowman *et al.*[23] to identify micronutrients that should be encouraged for use in the TBI population. We then designed a food plan to increase the probability of meeting or exceeding the RDAs for those micronutrients. This diet emphasizes non-starchy, colorful vegetables and berries and seaweed, and it restricts processed foods to ensure a maximally nutrient-dense diet. We routinely provide B vitamins and omega-3 fatty acids to patients who visit the TBI clinic. In addition, we routinely assess B vitamin levels and vitamin D status and correct any deficiencies that are discovered.

Limitations

The study does have important limitations that must be acknowledged. First, the nutritional assessment was completed using an FFQ rather than 24-hour dietary recalls. Because of recall bias, actual micronutrient intake may have been more or less than was calculated by the FFQs. Second, this was a small sample of predominantly Caucasian males. Finally, it is important to remember that this was an observational study.

Conclusion

Optimal brain health is associated with 14 different micronutrients with defined DRIs, including vitamins, minerals, antioxidants, and fats. However, there have been few studies regarding the nutritional adequacy of the diets of TBI outpatients. In our study, no patients consumed a diet that met or exceeded the RDAs of all the micronutrients. Encouraging the consumption of a more nutrient-dense diet, stressing non-starchy vegetables and berries, coupled with supplements such as B vitamin complex and omega-3

fatty acids may be beneficial for TBI outpatients. Our findings underscore that need for greater attention to the nutritional status of TBI patients in the outpatient setting. Prospective studies, using food plans and targeted supplementation specifically designed to ensure a plentiful supply of vitamins, minerals, antioxidants, and fatty acids required for optimal brain function should be carried out.

Appendix: Neurobehavior checklist

The following checklist was completed by the veterans at the time of their initial referral to the Polytrauma Clinic.

Please rate each of the following neurobehavioral symptoms on a 5-point scale 0 (*none: rarely if ever present; not a problem at all*) to 4 (*very severe: almost always present and I have been unable to perform at work, school, or home due to this problem; I cannot function without help*).

1. Feeling dizzy
2. Loss of balance
3. Poor coordination, clumsy
4. Headaches
5. Nausea
6. Vision problems, blurring, trouble seeing
7. Sensitivity to light
8. Hearing difficulty
9. Sensitivity to noise
10. Numbness or tingling on parts of my body
11. Change in taste or smell
12. Loss of appetite or increased appetite
13. Poor concentration, cannot pay attention
14. Forgetfulness, cannot remember things
15. Difficulty making decisions
16. Slowed thinking, difficulty getting organized, cannot finish things
17. Fatigue, loss of energy, getting tired easily
18. Difficulty falling or staying asleep
19. Feeling anxious or tense
20. Feeling depressed or sad
21. Irritability, easily annoyed
22. Poor frustration tolerance, feeling easily overwhelmed by things

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