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Research paper

The relationship between nutrient intake and executive function in adults with post-traumatic stress disorder

Kirsten Rowe [a,b,*], Erine Bröcker [a,c], Sharain Suliman [a,c], Renée Blaauw [d], Soraya Seedat [a,c], Leigh Luella van den Heuvel [a,c]

[a] Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa
[b] MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), University of the Witwatersrand, Johannesburg, South Africa
[c] South African Medical Research Council/Stellenbosch University Genomics of Brain Disorders Research Unit, Faculty of Medicine & Health Sciences, Stellenbosch University, Cape Town, South Africa
[d] Division of Human Nutrition, Department of Global Health, Stellenbosch University, Cape Town, South Africa

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ABSTRACT

Background: Executive function (EF) deficits are common in adults with post-traumatic stress disorder (PTSD). Macro- and micronutrient intake are potential modifiable factors that may influence EF in PTSD.
Objectives: To explore the relationship between the daily dietary intake of ω−3 and ω−6 polyunsaturated fatty acids (PUFAs), vitamin C, vitamin E, vitamin D, vitamin B12 and folate, and EF in adults with PTSD.
Methods: This was a cross-sectional observational study of adults with PTSD who completed neurocognitive assessments (n = 201). Digit span backwards, spatial span backwards, Stroop test and the Ruff Figural Fluency Task were used to assess EF. FoodFinder nutrient intake based on 24-h dietary recalls was used to calculate average daily nutrient intake. Multivariable linear regression models were used to regress EF on the nutrient variables.
Results: Intake of vitamin E, ω−3 PUFAs, and ω−6 PUFAs were all positively associated with planning and set-shifting, with vitamin E (adjusted $\beta = 0.20$, $p = 0.004$) and ω−6 (adjusted $\beta = 0.17$, $p = 0.01$) remaining significant after adjustment for age; sex; education and body mass index. Vitamin D intake was negatively associated with interference (adjusted $\beta = -0.21$, $p = 0.01$). Vitamin C, vitamin B12 and folate intake were not associated with EF.
Limitations: 24-h dietary recall data is limited by recall bias. Circulating nutrient levels were not measured.
Conclusions: Dietary intake of vitamins E, ω−3 and ω−6 may be important modifiable factors affecting EF in adults with PTSD. Randomised controlled trials are needed to investigate whether micro- and macronutrient interventions can improve EF and other outcomes in PTSD.

1. Background

Executive function (EF) denotes a set of cognitive control processes that use more basic cognitive abilities for problem-solving and planning towards meeting goals. It includes manipulation of information held in mind (working memory), the ability to switch between different tasks or strategies (cognitive flexibility) and inhibition (the ability to inhibit automatic responses in favour of responses supporting long-term goals; and the ability to ignore distractors or interfering stimuli [interference]) (Miyake et al., 2000). EF predicts educational attainment, health, finances, criminality, and treatment adherence (Ahmed et al., 2021; Moffitt et al., 2011; Polak et al., 2012). EF deficits are associated with externalising behaviours, including risk-taking and substance use (Young et al., 2009) and they are also common in post-traumatic stress disorder (PTSD) (Polak et al., 2012; Schuitevoerder et al., 2013). Although findings are mixed for working memory and planning, PTSD is associated with set-shifting, inhibition, and attention regulation deficits (Aupperle et al., 2012; Polak et al., 2012). Impaired inhibition has been associated with re-experiencing and hyperarousal severity (Aupperle et al., 2012). Furthermore, EF deficits may predispose people to developing PTSD and affect the maintenance of PTSD symptoms (Aupperle et al., 2012). Comorbid depression may also mediate the relationship

* Corresponding author at: Department of Psychiatry, Faculty of Medicine and Health Sciences, Francie van Zijl Drive, Parow, Cape Town 7505, South Africa.
E-mail address: kirstenrowe@gmail.com (K. Rowe).

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between PTSD and EF (Olff et al., 2014). Functional neuroimaging studies in PTSD show hyperactivation in limbic regions, especially the amygdala and insula, and hypoactivation of prefrontal cortices, including the ventromedial prefrontal cortex and anterior cingulate cortex. This may be associated with overactive 'emotional' processing networks directing attention towards threat-related stimuli, but underactive 'inhibitory' EF networks to disengage attention and direct it to the current task (Aupperle et al., 2012).

Macronutrient and micronutrient intake may affect EF. Greater mono- and polyunsaturated fatty acid intake have been associated with better cognition. High dietary intake of fibre and polyunsaturated fatty acids (PUFAs) are neuroprotective, promoting structural integrity (Muth and Park, 2021). Omega-3 (ω−3) fatty acids (particularly docosahexaenoic acid (DHA; C22:6), eicosapentaenoic acid (EPA; C20:5) and α-linolenic acid (ALA; C18:3)) are anti-inflammatory, inhibiting the conversion of reactive omega-6 (ω−6) arachidonic acid (C20:4) into pro-inflammatory factors, inhibiting leukocyte migration, and reducing T-lymphocyte proliferation.

Dietary antioxidants (e.g. vitamin C) scavenge free radicals in cell membranes and protect PUFAs from lipid peroxidation (Lewis et al., 2021), protecting against oxidative stress. Dietary antioxidants α-lipoic acid, vitamin E, zinc and polyphenols have all been associated with cognitive benefits (Lewis et al., 2021; Oroian et al., 2021; Rajaram et al., 2019). Vitamins B6, folate (B9) and B12 are crucial cofactors for one-carbon metabolism (folate and methylation cycles) (Lewis et al., 2021). Low levels of these vitamins are associated with high homocysteine, which is toxic to mitochondria. These pathways play a role in regulating epigenetic mechanisms, phospholipid synthesis, protein function, ribonucleic acid (RNA) metabolism, and monoamine neurotransmitter synthesis, and may thus also be important for EF. Vitamin D also plays a role in EF (Pettersen, 2017), and the brain's vitamin D receptor is involved in planning and processing (Lewis et al., 2021).

Nutrient intake is a potential modifiable factor affecting EF in adults with PTSD. PTSD is characterised by systemic inflammation (Oroian et al., 2021) including raised pro-inflammatory cytokines – interleukin (IL)-1β, IL-6, tumour necrosis factor-α, interferon-γ – and C-reactive protein (CRP) (Kim et al., 2020). Altered inflammatory markers are associated with structural and functional changes in brain regions responsible for regulating emotion and stress, including the amygdala, hippocampus and prefrontal cortex (Kim et al., 2020).[1]

PTSD is also often associated with metabolic comorbidities (Aaseth et al., 2019; Suliman et al., 2016), which may be mediated by oxidative stress, inflammation, one-carbon metabolism, elevated cortisol, and raised homocysteine levels (de Vries et al., 2015; Oroian et al., 2021; van den Heuvel et al., 2020). PTSD likely also involves immune dysregulation and changes in oxidative stress-related genes including brain-derived neurotrophic factor (BDNF) (Kim et al., 2020). The result is increased oxidative damage to membrane lipids and mitochondrial function, reduced endogenous antioxidant defence, and disturbed neurotransmitter signalling affecting cognition negatively (Du et al., 2016). Dietary antioxidants may thus be protective against these effects. As fatty acids are involved in neuronal membrane structure, inflammation regulation (ω−3 PUFAs are generally anti-inflammatory and ω−6 PUFAs pro-inflammatory), oxidative stress vulnerability and hypothalamic-pituitary-adrenal (HPA) axis activity (Mocking et al., 2018), higher ω−3 PUFA intake may be protective against psychiatric illness (Mocking et al., 2018). Lower ω−3 and higher ω−6 PUFA intake may lead to HPA axis hyperactivation and increased cortisol. These effects can further be aggravated as cortisol modulates enzymes involved in fatty acid production, mobilisation, and degradation, and increases oxidative stress, thereby reducing ω−3 PUFA levels (Mocking et al., 2018).

Oxidative stress and impaired antioxidant defences may explain cognitive deficits in PTSD (Ahmed et al., 2020; Dunlop and Wong, 2019; Wilson et al., 2013). Vitamin E acts as a free radical scavenger in rat models (Yatin et al., 2000), preventing memory impairment and affecting oxidative stress biomarkers and BDNF (Ahmed et al., 2020). Vitamin D supplementation has been associated with a reduced risk of suicide attempts and intentional self-harm in veterans and Vitamin D levels were also inversely associated with PTSD symptoms (Lavigne and Gibbons, 2023). Furthermore, different functional polymorphisms of the vitamin D-binding protein affect vitamin D levels and PTSD risk (Terock et al., 2020).

There is thus evidence for the role of macro- and micronutrients in relation to EF as well as PTSD. Whether macro and micronutrient intake are associated with EF in adults with PTSD has, however, not been directly investigated. This study aimed to explore the relationship between dietary intake of ω−3 and ω−6 PUFAs, vitamins C, D, E, B12, and folate, and EF in adults with PTSD. We hypothesised that there would be a positive association between the average daily dietary intake of these nutrients and EF in adults with PTSD.

2. Methods

2.1. Study design and setting

This study was a cross-sectional observational study nested within SHARED ROOTS, a case-control study in Cape Town, South Africa aiming to delineate the pathways contributing to comorbidity between selected neuropsychiatric disorders and metabolic syndrome (Swart et al., 2021; van den Heuvel et al., 2020). This study included PTSD cases without significant comorbidities who completed neurocognitive assessments (n = 201).

2.2. Participants

The source population was adults who self-identified as belonging to the South African mixed ancestry ethnic group who form 45.4 % of the Western Cape population (Malan-Muller et al., 2022). The SHARED ROOTS study was restricted to one ethnic group to limit the effects of population stratification on genomic analyses. The study inclusion criteria were: adults (≥18-years-old) willing and able to provide informed consent; able to read and write in English or Afrikaans; current PTSD diagnosis based on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) (as well as severity score ≥ 23); and participated in the neurocognitive assessment. Exclusion criteria were: pregnant currently; other serious psychiatric disorder (e.g. bipolar disorder or psychotic disorder on psychiatric history or Mini International Neuropsychiatric Interview [MINI] version 6.0); any significant medical or neurological disorder (e.g. HIV, systemic lupus erythematosus); alcohol or substance use disorder within the past six months (on the MINI); known intellectual disability; and history of a significant head injury.

2.3. Procedures

The main study made use of a multipronged purposive sampling strategy. Patients were recruited from May 2014 until June 2017 primarily via print advertisements with additional recruitment via public health facilities within the Tygerberg Hospital catchment area.

All participants were assessed over two to three study visits at Tygerberg Campus. Diagnostic, clinical and participant self-administered measures were completed at the first visit. Neurocognitive assessments, physical procedures and lifestyle measures occurred at the second visit 1–4 days later. If assessments could not be completed within two visits, additional visits were arranged as required.

[1] EF = executive function; PTSD = post-traumatic stress disorder; PUFA = polyunsaturated fatty acids; ω−3 = omega-3; ω−6 = omega 6; IL = interleukin; CRP = C-reactive protein; HPA axis = hypothalamic-pituitary-adrenal axis; BDNF = brain-derived neurotrophic factor.

2.4. Outcomes and measures

2.4.1. Nutritional variables

The daily dietary nutrient intake was estimated using the 24-h dietary recall and a food indicator list. Estimated food-only intake of each nutrient was quantified from 24-h dietary recall using FoodFinder, software that determines the nutritional value of South African foods (https://foodfinder.samrc.ac.za/). The procedure for the 24-h recall included: listing of foods and beverages ingested by the participant in the previous 24 h; detailed descriptions of foods, food brands where relevant, food preparation methods, quantity ingested; and final checks for any forgotten foods. Food portion size estimation was done using ordinary household measures and food pictures from the Dietary Assessment and Education Kit (Steyn and Senekal, 2004). Food portion estimates were converted to grams with the MRC Food Quantities Manual (Langenhoven et al., 1991). Nutritional data is described using Dietary Reference Intakes (DRI) (Otten et al., 2006).

2.4.2. Cognitive variables

Verbal working memory was measured using the digit span backwards and visuospatial working memory using the spatial span backwards, both tasks from the Wechsler Memory Scale — Third Revision (WMS-III) (Wechsler, 1997). These tasks are frequently used as working memory measures and have been used successfully in South Africa (Robbins et al., 2018). Digit span (forwards and backwards) has been validated in South African adults (Rowe et al., 2021; Singh et al., 2010). In the digit span task, participants were asked to recall a series of digit sequences of increasing length that were read aloud by the interviewer. The baseline forwards condition, repeating numbers in the same order as that read by the interviewer, occurred first with two different sequences of each length (from two-digit sequences up to nine-digit sequences). This was followed by the backwards condition in which numbers were repeated in reverse order (from two-digit sequences up to eight-digit sequences). In the analogous visuospatial version of the task, the spatial span, there were also two attempts at each sequence length. The forwards condition occurred first with the touching of sequences of numbered blocks in the same order as the interviewer (from two-block to nine-block sequences). This was followed by the backwards condition in which participants had to touch the sequence of numbered blocks in the reverse order to that of the interviewer (from two-block to nine-block sequences).

Interference was measured using the Stroop colour and word test incongruent raw score (Golden and Freshwater, 1978). There are preliminary normative values in a small South African sample (Andrews et al., 2012). It taps the ability to inhibit the cognitive interference that occurs when processing two distinct stimulus features (e.g. reading the word, naming the ink colour the word is written in) simultaneously, the so-called Stroop Effect (Scarpina and Tagini, 2017). The incongruent raw score (the number of incorrect responses subtracted from the number of correct responses) was used. The Stroop task involved three conditions, each needing to be completed as quickly and accurately as possible. There were two baseline conditions – word (reading the names of three colours – red, green and blue – for 100 words) and colour (reading the three ink colours – red, green and blue – for 100 words), followed by the test condition, the colour-word condition in which the word and ink colour were incongruent (e.g. blue written in red ink) and the ink colour of each of 100 words needed to be called out.

Planning and set-shifting were measured using the Ruff Figural Fluency Test (RFFT) total unique designs raw score. This task is a non-verbal measure of EF that has been used in South African adults previously (Thornton et al., 2008). There are five different dot configurations that participants connect. The participant draws as many unique designs as possible within 1 min for each dot configuration by connecting the dots in various patterns. The main score is derived from the total number of unique designs. In the original validation study with healthy adults, the test-retest reliability was high for the main score (correlation coefficient 0.76) (Ruff et al., 1987).

Global EF was determined by combining all four cognitive variables (verbal working memory, visuospatial working memory, cognitive interference, planning, and set-shifting).

2.4.3. Other variables

Age (in years), sex, highest education level (successfully completed years), employment status (employed for most of the prior 12 months), and marital status were measured with a demographic questionnaire. Body mass index (BMI) was calculated from physically measured weight and height.

2.5. Ethical aspects

The Shared Roots study (N13/08/115) and the substudy reported here (S22/08/162) were approved by the Stellenbosch University Health Research Ethics Committee. All participants provided written informed consent for participation. Participants were able to withdraw consent at any stage. An appropriate referral plan to community clinics was in place for participants who became unduly distressed during interviews, showed signs of a medical or psychiatric condition requiring further clinical management, or endorsed suicidal ideation. Participants with newly diagnosed metabolic abnormalities underwent lifestyle counselling by the study nurse before referral for further management.

2.6. Statistical analysis

Due to the main study being a multi-omics study, the sample size for the main study was estimated. The achieved power (calculated using G*Power 3.1.9.4) for this study was 0.29 (low) to detect a small effect size ($f^2 = 0.02$) and 0.99 (high) to detect a medium effect size ($f^2 = 0.15$) given a multivariable linear regression with five predictors, an alpha of 0.05, and a sample size of 201.

The FoodFinder dietary nutrient intake was used to calculate the total daily nutrient intake for each variable. Standardised versions of the four neurocognitive scores were combined using an exploratory factor analysis (principal factors method with orthogonal varimax rotation) with the first factor retained as a 'global executive function score'. This was used as a dependent cognitive variable. In additional exploratory sub-analyses, each of the four specific neurocognitive scores was regressed on the nutrient predictor variables. The initial 24-h food recall calculated intake represented the observed intake distributions for energy and nutrients. The second 24-h food recall data from a random subset of 15 % of the sample were used to make adjustments to the observed intake distributions to remove the within-person variability partially and estimate the usual nutrient intake distribution (Subcommittee on Interpretation and Uses of Dietary Reference Intakes and Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 2003).

Simple bivariable linear regression models were initially built followed by multivariable linear regression models in which the global and specific EF scores were regressed on the estimated daily food intake of: vitamin C (milligrams [mg]); vitamin E (mg); ω−3 polyunsaturated fatty acid (PUFA) (C18:3, C20:5, C22:5 and C22:6) (grams [g]), ω−6 PUFAs (C18:2 and C20:4) (g); vitamin D (micrograms [mcg]); vitamin B12 (mcg); folate (mcg).

The following control variables were included in the adjusted models: age; sex; education level; and BMI. Findings from both unadjusted and adjusted models are presented. Regression diagnostics revealed that the errors in each model met the assumptions of normality and homogeneity of variances for the use of ordinary least squares linear models. Additionally, there was no evidence for multicollinearity or model misspecification.

All data was analysed using StataSE Version 14. All hypothesis tests were two-tailed. The alpha level for significance was set at 0.05. No corrections were made for multiple comparisons given the exploratory

nature of this study.

3. Results

3.1. Participants, descriptive and outcome data

There were 201 participants in this study. In the main study, there were 307 participants with PTSD but 106 of those participants were excluded from this study (see Fig. 1). Summary descriptive, mental health, cognitive, and nutritional data are presented in Table 1. More than 80 % of the sample were below the DRI for daily dietary intake of vitamin C, vitamin E, ω−3 PUFAs, vitamin D, and folate.

See Table 2 for regression results. Intake of vitamin E, ω−3, and ω−6 were all positively associated with planning/set-shifting in unadjusted analyses, with vitamin E (adjusted $\beta = 0.20$, $p = 0.004$) and ω−6 (adjusted $\beta = 0.17$, $p = 0.01$) remaining significantly positively associated with planning/set-shifting after adjustment for potential confounders. Vitamin D intake was negatively associated with interference before and after adjustment for confounders (adjusted $\beta = -0.19$, $p = 0.006$), and negatively associated with global EF on adjusted analysis only (adjusted $\beta = -0.13$, $p = 0.05$). Vitamin C, vitamin B12, and folate intake were not associated with EF.

4. Discussion

4.1. Key results

PTSD is an inflammatory disease commonly marked by comorbid metabolic disease. Systemic dysregulation in metabolism, inflammation, and mitochondrial function may be useful novel targets for treating PTSD symptoms, including executive dysfunction in patients with PTSD (Bersani et al., 2020; Miller et al., 2018). Dietary intake of certain nutrients that modulate inflammatory and metabolic processes and oxidative stress may be important modifiable factors of the EF of adults with PTSD.

In contrast to our hypothesis, there was no association between vitamin C intake and EF. This may be because we did not account for vitamin C supplementation and the generally low dietary intake of the sample relative to the DRI. Aligned with our hypothesis, there was a positive association between antioxidant vitamin E intake and planning/set-shifting. Antioxidants (including vitamin E, vitamin C, and α-lipoic acid) have shown microvascular and autonomic benefits in young adults with PTSD (Weggen et al., 2021). Antioxidants have also demonstrated cognitive benefits when administered to rats in a PTSD-like behaviour model and protected against reduced BDNF levels (Ahmed et al., 2020). They have been associated with cognitive benefits in humans as well (Lewis et al., 2021). Our findings with regard to antioxidant vitamins thus partially align with the literature.

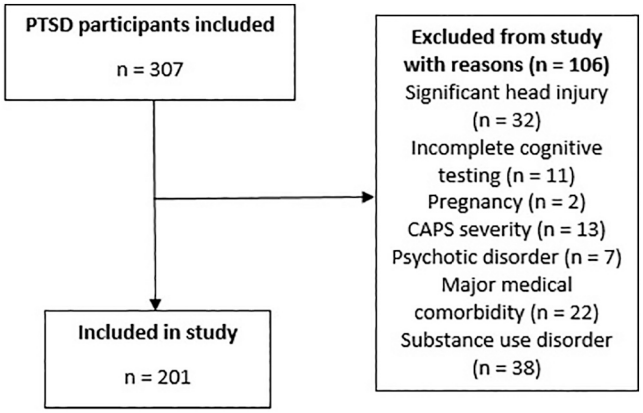

Fig. 1. Flow diagram showing study participant inclusion and exclusion.

Table 1
Summary of participant sociodemographic, cognitive, and nutritional data.

Variables	Values
Sociodemographic variable	N (%) unless specified
Age, mean (SD)	41.1 (12.0)
Female sex	158 (78.6)
Highest level of education, mean (SD)	10.8 (2.4)
Body mass index (kg/m^2), median (IQR)	29.4 (24.2–35.5)
Employed	73 (36.3)
Marital status	
Never married	63 (31.5)
Currently married or cohabiting	88 (44.0)
Separated, divorced, or widowed	49 (24.5)
Mental health variables	N (%)
Comorbid anxiety disorder or obsessive-compulsive disorder on MINI	92 (45.8)
Comorbid major depressive disorder on MINI	62 (30.9)
On therapeutic dose of antidepressant	26 (12.9)
Cognitive variables	Mean (SD)
Verbal working memory: Digit span backwards raw score	4.9 (2.0)
Visuospatial working memory: Spatial span backwards raw score	6.1 (2.2)
Interference: Stroop colour-word test interference raw score	26.3 (9.6)
Planning: Ruff figural fluency test total unique designs raw score	57.9 (17.6)
Global executive function score	0.02 (0.7)

Nutritional variable	Dietary Reference Intakes (DRIs)	Median total daily nutrient intake (IQR)	Percentage below DRI
Vitamin C (mg/d)	Males: 75 Females: 60	Males: 28.4 (18.3–43.8) Females: 26.2 (17.3–39.7)	Males: 88.4 Females: 87.3 Full sample: 87.6
Vitamin E (mg/d)	12	6.8 (5.3–8.9)	92.0
ω−3 PUFAs (g/d)	AMDR: 0.6–1.2	0.4 (0.3–0.5)	82.1
ω−6 PUFAs (g/d)	AMDR: 5–10	11.1 (7.6–17.9)	9.5
Vitamin D (mcg/d)	≤50-years: 5 51–70: 10 >70: 15	≤50-years: 2.4 (1.9–3.5) 51–70: 2.4 (1.8–3.1) >70: 2.9 (single value)	≤50-years: 92.5 51–70: 100.0 >70: 100.0 Full sample: 94.5
Vitamin B12 (mcg/d)	2.0	2.8 (2.1–3.6)	20.9
Folate (mcg/d)	320	186.9 (146.1–229.9)	93.5

Key: AMDR = acceptable macronutrient distribution range; DRI = Dietary Reference Intake; g/d = grams per day; IQR = interquartile range; kg/m^2 = kilograms per square metre; mcg/d = micrograms per day; mg/d = milligrams per day; MINI = the Mini International Neuropsychiatric Interview; N = number; ω−3 = omega-3; ω−6 = omega-6; PUFA = polyunsaturated fatty acid; SD = standard deviation.

Given that PTSD is characterised by systemic inflammation including elevated pro-inflammatory cytokines and CRP, a higher intake of anti-inflammatory nutrients such as ω−3 PUFAs may be protective (Mocking et al., 2018). Lower ω−3 PUFA intake may lead to HPA axis hyperactivation with resultant hypercortisolaemia, increasing oxidative stress, which leads to further reductions in bodily ω−3 PUFA levels (Mocking et al., 2018). In rat models of PTSD-like behaviour, ω−3 PUFA supplementation was beneficial for cognition, preventing memory impairment (Alquraan et al., 2019). Although we found a significant positive association between ω−3 PUFA intake and planning, this association was no longer significant after adjustment for potential confounders. We did, however, find a positive association between ω−6

Table 2
Summary of regression analysis results.

Variables	Global EF		Verbal WM		Visuospatial WM		Interference		Planning	
	Unadj. β	Adj. β	Unadj. β	Adj. β	Unadj. β	Adj. β	Unadj. β	Adj. β	Unadj. β	Adj. β
Vitamin C	−0.01 (p = 0.87)	0.01 (p = 0.83)	0.001 (p = 0.99)	0.02 (p = 0.79)	−0.02 (p = 0.74)	−0.01 (p = 0.90)	0.02 (p = 0.73)	0.05 (p = 0.44)	−0.06 (p = 0.40)	−0.95 (p = 0.47)
Vitamin E	−0.01 (p = 0.94)	−0.01 (p = 0.89)	−0.07 (p = 0.33)	−0.07 (p = 0.32)	0.05 (p = 0.51)	0.04 (p = 0.58)	−0.09 (p = 0.21)	−0.09 (p = 0.20)	0.20 (p = 0.005)*	0.20 (p = 0.004)*
Omega-3 PUFA	0.06 (p = 0.37)	0.04 (p = 0.59)	0.003 (p = 0.96)	−0.02 (p = 0.78)	0.09 (p = 0.21)	0.06 (p = 0.40)	−0.01 (p = 0.93)	−0.01 (p = 0.91)	0.14 (p = 0.04)*	0.12 (p = 0.09)
Omega-6 PUFA	0.07 (p = 0.32)	0.05 (p = 0.48)	0.02 (p = 0.81)	0.003 (p = 0.97)	0.06 (p = 0.37)	0.04 (p = 0.58)	0.002 (p = 0.98)	−0.01 (p = 0.89)	0.19 (p = 0.006)*	0.17 (p = 0.01)*
Vitamin D	−0.12 (p = 0.10)	−0.13 (p = 0.05)*	−0.11 (p = 0.10)	−0.11 (p = 0.10)	−0.04 (p = 0.61)	−0.05 (p = 0.47)	−0.17 (p = 0.02)*	−0.19 (p = 0.004)*	0.07 (p = 0.33)	0.06 (p = 0.39)
Vitamin B12	−0.02 (p = 0.76)	−0.01 (p = 0.93)	−0.01 (p = 0.86)	0.01 (p = 0.92)	−0.01 (p = 0.92)	0.01 (p = 0.90)	0.002 (p = 0.98)	−0.001 (p = 0.98)	−0.07 (p = 0.30)	−0.06 (p = 0.36)
Folate	−0.04 (p = 0.57)	−0.02 (p = 0.73)	−0.12 (p = 0.08)	−0.09 (p = 0.23)	−0.01 (p = 0.85)	0.001 (p = 0.98)	0.04 (p = 0.56)	0.02 (p = 0.78)	0.01 (p = 0.90)	0.02 (p = 0.74)

Key: The coefficients and probability (p) values are from ordinary least squares linear regression models containing each food-only nutrient variables (independent) and the cognitive variable (dependent). The adjusted models additionally include the following control variables: age, gender, highest education level, BMI (body mass index); EF = executive function; WM = working memory; unadj. = unadjusted; adj. = adjusted; df = degrees of freedom; β = standardised beta coefficient; p = probability value; PUFA = polyunsaturated fatty acids.
* $p \leq 0.05$.

PUFA intake and planning/set-shifting which remained significant after adjustment. A possible reason may be that almost the entire sample (82.1 %) had an ω−3 PUFA intake below the DRI, while only 9.5 % had an ω−6 PUFA intake below the DRI.

Vitamin D intake was negatively associated with interference. There was no association between vitamin D intake and global EF; however, a weak association emerged after accounting for confounders. Given that the brain's vitamin D receptor is involved in processing and planning ability, we had predicted that vitamin D intake would be positively associated with EF (Lewis et al., 2021). PTSD may also be associated with an altered vitamin D metabolism and vitamin D deficiency (Terock et al., 2020) suggesting that higher vitamin D intake might be useful in this population. A trial of vitamin D supplementation in healthy adults resulted in better visual (non-verbal) memory, particularly in those who were deficient at baseline (Pettersen, 2017). Our results thus contrast with the literature; however, it may be because the sample generally had a low vitamin D intake relative to the DRI and we did not account for vitamin D supplementation. Furthermore, dietary vitamin D is not the only source of vitamin D in the body. The body also produces its own vitamin D in the skin.

Folate and vitamin B12 are protective of mitochondrial functions and crucial cofactors for the folate and methylation cycles which play a role in regulating epigenetic mechanisms, phospholipid synthesis, protein function, RNA metabolism, and monoamine neurotransmitter synthesis. They have both been found to have beneficial effects on cognition (Lewis et al., 2021); however, in this study, no association was found between the dietary intake of folate or vitamin B12 and EF. Folate intake was generally low in the sample compared to the DRI.

Increasing intake of various nutrients simultaneously may result in synergistic effects. A randomised controlled trial in cognitively healthy adults ≥65-years-old showed that two years of supplementation with ω−3 PUFAs, vitamin E, and carotenoids improved working memory in a dose-dependent way (Power et al., 2022). The combined effects of the intake of various nutrients were not explored in this study but should be explored in future studies in adults with PTSD.

4.2. Limitations

There are several limitations pertaining to this study. Participants may have completed their food recall inaccurately due to recall bias. The 24-h food recall may not accurately reflect an individual's dietary pattern if that day was not representative of a typical day or if the individual's diet varies considerably from day-to-day. 24-h dietary recall data may generally provide less reliable data regarding micronutrient intake than for macronutrient intake. To improve the accuracy of the estimates, the food recall was administered twice, and data from a representative subset of participants was used so that adjustments for within-person variability could be made for the whole sample to estimate the usual intakes from the observed intakes. There was limited data on participants' nutrient supplement intake, so we were not able to account for supplement intake in the analysis. Exclusion of these unavailable data may have biased the findings. We did not analyse for effects of specific combinations of nutrients; however, given the small effect sizes found in our study, it would make sense to consider combining nutrients in an intervention study to create the potential for a larger overall effect size. Multiple comparisons may have increased the risk of false positive findings, particularly with an alpha of 0.05. Given the limited existing data on this subject, this study was exploratory to generate further hypotheses for future replication in other studies.

Our study was conducted in a South African population and results may not be generalisable to other geographic regions or ethnic groups. Given the female predominance of the sample, the findings may not generalise as well to males with PTSD. Most of the sample were overweight or obese and had low intake of vitamins C, D, E, ω−3 PUFAs and folate. Generally, deficient intake of these micronutrients might have influenced the findings in the relevant analyses. Furthermore, we only evaluated dietary intake of nutrients and did not determine circulating levels of the nutrients. Due to the stringent exclusion criteria, these findings may not apply to adults with PTSD with significant medical and psychiatric comorbidities, including substance use disorders which are relatively common in adults with PTSD.

5. Conclusions

Average daily dietary intake of vitamin E, ω−3 PUFAs, and ω−6 PUFAs were all positively associated with planning/set-shifting, but not global EF. The negative associations between vitamin D intake, and interference and global EF might have been caused by not accounting for high-dose vitamin D supplementation as well as other sources of vitamin D in the body. We found that most adults with PTSD in our sample had deficient intake of the micronutrients investigated in this study, as well as low ω−3 PUFA intake. This, alongside high rates of obesity, suggests generally poor nutrition in people living with PTSD in our setting. Poor nutrition may be one of the lifestyle factors that contribute to the increased rates of metabolic syndrome and cardiovascular disease observed in people with PTSD (Mellon et al., 2018). Our results

highlight the importance of addressing lifestyle factors that contribute to poorer health outcomes in people with PTSD.

This study provides preliminary evidence on the potential role, albeit with small effect sizes, of the intake of specific nutrients in EF in adults with PTSD in South Africa. Vitamin E, ω−3 PUFA and ω−6 PUFA intake may be important modifiable factors affecting EF in adults with PTSD. Randomised controlled trials are needed to investigate whether supplementation or a diet high in any of these nutrients can improve EF in PTSD, and if so, potential dose-response relationships. Findings from such trials could help treating clinicians who are managing patients with PTSD make nutritional recommendations, for example regarding nutritional supplements and/or dietary recommendations. This could serve as a possible therapeutic augmentation strategy in adults with PTSD, particularly those with EF deficits. Future intervention research can explore if this might have protective downstream effects on PTSD symptoms affected by EF and other important outcomes.

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CRediT authorship contribution statement

Kirsten Rowe: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Erine Bröcker:** Writing – review & editing. **Sharain Suliman:** Writing – review & editing. **Renée Blaauw:** Supervision, Writing – review & editing. **Soraya Seedat:** Funding acquisition, Methodology, Resources, Supervision, Writing – review & editing. **Leigh Luella van den Heuvel:** Conceptualization, Data curation, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The views expressed in this manuscript belong to the authors and are not the official position of the institution or funder. No potential conflicts of interest were reported by the authors.

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