Short-term effects of a Mediterranean-style dietary pattern on cognition and mental well-being: a systematic review of clinical trials

Latife Esgunoglu[1]*, Amy Jennings[1], Elizabeth Sanchia Connole[2], Karen Joy Murphy[2] and Anne Marie Minihane[1]

[1]*Department of Nutrition and Preventive Medicine, Norwich Medical School, University of East Anglia, Norwich, UK*
[2]*Department of Nutrition and Dietetics, Clinical and Health Sciences, University of South Australia, Adelaide, Australia*

Abstract

Although the long-term effects of a Mediterranean-style dietary pattern (MDP) on cognition and overall mental well-being have been consistently described, the short-term effects of the MDP on cognitive performance, mood and anxiety have not been as widely reviewed. Therefore, the aims of this systematic review were to synthesise the evidence from randomised controlled trials (RCT), to examine whether a MDP can alter cognition and overall mental well-being in the short-term (up to 10 d). This will also be used to identify research gaps and to inform the design of future acute RCT in the area. Ovid Embase, Ovid MEDLINE and Web of Science Core Collection were searched from inception to 8 December 2020. The data were synthesised narratively with no quantitative synthesis. The detailed protocol is available on PROSPERO, with the registration number CRD42021221085. A total of 3002 studies were initially identified. After the deduplication and screening stages, four studies (three articles and one conference proceeding) were eligible to be included. Despite the very limited data obtained, the literature suggests that a MDP can improve cognition and mood in the short-term. Specifically, improvements in attention, alertness and contentment were consistently reported. A MDP appears as a promising strategy to improve short-term cognitive and mental health. A limitation of this review is the small number of studies identified; therefore, future studies are required to confirm these initial novel findings and to provide granularity as to which domains are most responsive and in which population subgroups.

Key words: Mediterranean-style dietary pattern: Mood: Cognition: Acute: Short-term

With global ageing population demographics, the prevalence of cognitive disorders has surged[1]. The number of individuals living with dementia, which is a major cause of loss of independence and disability in older age, has doubled between 1990 and 2016, reaching 50 million worldwide[1]. In the UK, dementia is now the number one cause of death, responsible for about 15 % of all-cause mortality[2]. Besides, dementia has an enormous economic burden, with the global cost expected to reach $2 trillion by 2030[3].

The prevalence of mild cognitive impairment, the transition phase prior to incident dementia, has been estimated to occur in 15–20 % of the population aged over 60 years, with 8 %–15 % progressing to dementia per year[4]. Subjective memory complaints (SMC), which are loosely defined as a state in which individuals present with 'self-reported' cognitive decline relative to their previous cognitive status (which is not diagnosed by objective standard tests), occur in 50–80 % of individuals aged 70 years or older[5]. SMC is linked to depression, anxiety and future Alzheimer's disease risk[5,6]. In addition to cognitive decline, mental disorders, including depression and anxiety disorders, are prevalent, occurring in 3–5 % of the global population[7], and are one of the top three causes of non-fatal health loss in terms of years lived with disability[8]. Depression is also a risk factor for future dementia[9].

Currently, Alzheimer's disease and other dementias are irreversible with no effective treatments available to slow or reverse the condition. Therefore, behaviours (such as altered eating behaviour and nutrition status) which can prevent or delay progression of these conditions have the potential to dramatically reduce both individual risk and the population burden of the disease[10]. A Mediterranean-style dietary pattern (MDP) is emerging as having potential positive effects on mental health status. The diet is characterised by high consumption of extra virgin olive oil (EVOO) and plant-based foods such as fruits, vegetables, nuts, legumes, whole-grain cereals; low to moderate consumption of dairy products mainly yoghurt and cheese; fish

consumed two to four times a week; low amounts of red meat and moderate consumption of red wine mainly with meals[11]. EVOO, in addition to being the major component of a MDP, has been shown to independently confer neuropsychiatric and cardiovascular benefits[12], attributed to its high monounsaturated fatty acids (MUFA) and phenolic content[13].

The cardiometabolic health benefits of a MDP, first reported in the Seven Countries Study in the 1950s[14], are now well established[15–17]. An improved cardiometabolic phenotype is thought to in part underlie the emerging cognitive benefits of this dietary pattern. However, the majority of this evidence has been acquired from observational studies, such as European Prospective Investigation into Cancer-Norfolk[18], with a dearth of randomised controlled trials (RCT) which report on the causal benefits of a MDP on long-term cognitive and overall mental health. The Prevencion con Dieta Mediterranea (PREDIMED) was the first RCT testing the long-term effectiveness of a MDP in primary prevention which had incidence of CVD as the primary point[19]. In a sub-group secondary analysis, the MDP interventions enriched with either EVOO or nuts were shown to improve cognitive function[20] and depressive symptoms[21]. Available systematic reviews and meta-analysis focus on the long-term mental health benefits of a MDP, with adherence associated with an overall risk ratio of 0·79 (95 % CI 0·70, 0·90) of developing cognitive disorders[22]. Although no association was observed in the cohort analysis, data from nine cross-sectional studies indicate a negative relationship between adherence to a MDP and risk of depression (OR = 0·72; 95 % CI 0·60, 0·87)[23].

In addition to the long-term trajectory, for the ever-increasing number of individuals with pre-existing cognitive or mental health deficits and even in healthy individuals, there is a great need and interest in identifying nutrition strategies which improve cognition, mood and anxiety in the short-term, in order to improve capabilities, independence and overall quality of life. Therefore, the objectives of the current systematic review are, (i) to conduct an evidence synthesis from RCT data to scrutinise whether a MDP has the potential to alter cognition, mood and mental well-being in the short-term and (ii) identify research need and inform the design of future acute RCT in the area.

Methods

This systematic review was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[24]. Our systematic review protocol is available on PROSPERO with the registration number CRD42021221085[25].

Search strategy, eligibility criteria and study selection

'Short-term' is defined as 'up to 10 days' by discussions among the authors, where effects on cognition are likely to be mediated by rapidly responsive physiological processes such as brain blood flow, inflammation and oxidative status. Ovid Emabse, Ovid MEDLINE and Web of Science Core Collection were searched[26,27] from their inception dates to 8 December 2020 by using keywords covering 'Mediterranean diet', 'olive oil', 'cognition', 'dementia', 'mood', 'mood disorders', 'anxiety', 'anxiety disorders', 'depression', 'depressive disorders' and 'well-being'. Free search terms and medical subject heading terms were combined where the databases allowed, namely Embase and MEDLINE. Final search strategies were constructed with the assistances of an expert in systematic reviews in Norwich Medical School, and the academic librarian of the Faculty of Medicine and Health Sciences, University of East Anglia. The full electronic search string used in Ovid Embase is presented in Appendix 1.

Studies were accepted eligible if they,

- had an RCT design,
- intervened with either a MDP or EVOO,
- had an intervention period of up to and including 10 d,
- assessed either cognition, mood, anxiety or depression as a primary or secondary endpoint,
- included adults over 18 years and
- published in the English language.

Observational epidemiological studies were excluded. No sex filter was applied. The reference lists of included studies were manually read in order to obtain further potential publications. Two authors (L. E. and E. S. C.) independently completed screening the titles and abstracts against the predefined eligibility criteria. Any discrepancies were resolved by discussions until an agreement was reached. EndNote X9 is used as the reference management tool.

Definition of cognitive and mental health as the primary outcomes

Cognition is defined as 'the mental action or process of acquiring knowledge and understanding through thought, experience and the senses'[28]. Memory, attention, reasoning, decision-making, visual and spatial abilities and behaviours are examples of 'cognitive functions'. Depression and anxiety are significant mood disorders; however, mild to moderate level of psychological stress can also cause substantial reductions in the quality of life. A variety of validated tools are available to assess cognition and mood, with details of the tools used in individual studies detailed below and in Table 1.

Data extraction and quality assessment

A table which recorded the authors, publication year, country where studies were conducted in, type of RCT, participant characteristics, study duration, intervention, main outcomes, assessment methods used, results (mental health status) and additional results/comments was generated to extract the data from the included studies.

A quality assessment was done using RoB2, a revised tool for risk of bias by Cochrane[29], which has five domains: bias arising from the randomisation process (D1), bias due to deviations from intended interventions (D2), bias due to missing outcome data (D3), bias in measurement of the outcome (D4), bias in selection of the reported result (D5) and plus overall bias (D6). The results of bias investigation are presented by means of a traffic light plot under low risk, some concerns or high risk.

Table 1. Study details and main outcomes
(Mean values and standard deviations)

Authors	Publication year	Country	Type of RCT	Participant characteristics	Duration	Intervention	Main outcomes	Assessment methods used	Additional outcomes	Results (Mental Health Status)	Additional results/ comments
Diekmann et al.[29]	2019	Germany	Crossover	n 26 8 Female, 18 Male Metabolic syndrome 69·9 (SD 4·7) years* BMI = 30·3 (SD 2·3) kg/m2*	4·5 h, 2-week washout periods	4 interventions (isoenergetic, 4300 kJ/ meal): 1. WD + walking. 2. WD + resting. 3. MDP + walking. 4. MDP + resting	Mood, Cognition	MDMQ[34], FAIR-2[37]	Appetite, Plasma cortisol levels	MDMQ: No effect of diet FAIR-2: Walking group: 1·4-fold increase in attention in MDP compared with WD. Resting group: 1·1-fold increase in attention in MDP compared with WD. ($P = 0.045$ from iAUC data, meal × time interaction NS).	No effect of diet on cortisol. VAS: No impact of diet on hunger. Satiety was higher after MDP compared with the WD ($P < 0.001$)
de Vries et al.[30]	2017	Netherlands	Parallel arms	n 53 Female 22·3 (SD 3·6) years*	10 d	MDP or control group	Mood	POMS[35], Bond–Lader[36]		Significant decreases in vigour/activity ($P < 0.001$); tension/anxiety ($P = 0.001$); fatigue/inertia ($P = 0.003$); anger/hostility ($P = 0.014$); confusion/bewilderment ($P = 0.015$) and the total mood disturbance score (p not stated), and contentment ($P = 0.001$); alertness ($P = 0.003$) in MDP compared to control group. *P* values are for the time × treatment interactions, no effect sizes are presented.	Food diaries were used over 10 d but not reported in the text. No detail given on the control group diet.
Lee et al.[31]	2015	Australia	Crossover	n 24 Female Healthy	10 d	MDP or NC	Mood, Cognition	POMS[35], Bond–Lader[36], COMPASS[38]	Cardiovascular function: blood pressure, blood flow velocity and arterial stiffness, Dietary adherence, Anthropometric measures	Confusion reduced in MDP (−1·19) and increased (1·52) in NC ($F = 6.87$, $P = 0.02$) Alertness increased in MDP (6·93) and reduced in NC (−8·31) ($F = 14.11$, $P < 0.01$) Contentment increased in the MDP group (5·35) and reduced in NC (−4·23). ($F = 6.49$, $P < 0.02$). Immediate word recall: Correct responses increased in MDP (1·14) and reduced in NC (−0·64) ($F = 8.19$, $P = 0.01$). Incorrect responses decreased in MDP (−0·32) and increased in NC (0·36) ($F = 4.83$, $P = 0.04$).	Food diaries were used over 10 d Augmentation pressure (mmHg) reduced in MDP (−1·05) and increased in NC (0·95) ($F = 6.15$, $P = 0.02$) 100 % dietary adherence to MDP BW: Reduced in MDP group (−1·77 kg) and increase in NC group (0·11) ($F = 10,81$, $P < 0.01$)

Table 1. (*Continued*)

Authors	Publication year	Country	Type of RCT	Participant characteristics	Duration	Intervention	Main outcomes	Assessment methods used	Additional outcomes	Results (Mental Health Status)	Additional results/comments
				25·6 (SD 5·1) years[*]						Delayed word recall: Incorrect responses decreased in MDP (−0·33) and increased in NC (0·71) ($F = 4\cdot57$, $P = 0\cdot046$).	No change in BMI
										3-back task: Correct responses reduced in the MDP (−2·32) and increased in NC (4·14) ($F = 6\cdot64$, $P = 0\cdot02$).	
Mc Millan et al.[32]	2011	Australia	Parallel arms	n 25	10 d	MDP or NC	Mood, Cognition	65-item POMS[35], Bond–Lader[36], COMPASS [38]	Dietary adherence, Anthropometric measures	Vigour increased in MDP by 18 % (3·67) and reduced in NC by 22 % (−5·06) ($F = 11\cdot25$, $P = 0\cdot003$)	Food diaries were used over 10 d
										Alertness increased in MDP by 30 % (16·43) and reduced in NC group by 15 % (−9·02) ($F = 22\cdot23$, $P < 0\cdot001$). Contentment increased in MDP by 20 % (12·89) and reduced in NC by 15 % (−10·4) ($F = 16\cdot634$, $P < 0\cdot001$)	100 % dietary adherence to MDP
				Female						Numeric working memory: RT increased in MDP by 2 % (+15) and decreased in NC group by 14 % (−122) ($F = 5\cdot05$, $P = 0\cdot04$)	
				Healthy						Corsi Blocks task: RT reduced in MDP by 14 % (−420) and increased in NC by 27 % (837) ($F = 17\cdot628$, $P < 0\cdot001$)	No effect of diet on BW, BMI and WC.
				21·1 (SD 3·3) years[*]						Word recognition: RT reduced in MDP by 3 % (−29) ($P = 0\cdot574$, NS) and in the NC by 20 % (−191) ($P = 0\cdot001$). The difference between groups was significant: ($F = 5\cdot04$, $P = 0\cdot035$).	

RCT, randomised controlled trial; WD, Western diet that is rich in total fat, SFA, saturated fatty acids; and animal protein; MDP, Mediterranean-style dietary pattern; MDMQ, Multidimensional Mood State Questionnaire for mood; FAIR-2, Frankfurt Attention Inventory-2 for cognition; iAUC: AUC, area under the curve; VAS, Visual Analogue Scale for hunger, appetite and satiety; POMS, Profile of Mood States questionnaire for mood (tension/anxiety, anger/hostility, fatigue/inertia, vigour/activity, confusion/bewilderment, depression/rejection and total mood disturbance score); Bond–Lader Scale for mood (alertness, contentment and calmness); NC, No change in diet; COMPASS, The Computerised Mental Performance Assessment System for cognitive domains; RT, reaction time; BW, body weight; WC, waist circumference.
* Represents mean and standard deviation unless otherwise stated.

Data synthesis

A narrative approach was used to synthesise the data. No quantitative analysis was performed due to the small number of studies.

Results

Study identification

Initially, 3002 studies were obtained from the three electronic databases. After deduplication, 2261 studies remained, with 1721 from the MDP search and 540 from the EVOO search. Of these, 2253 were excluded following the title and abstract screening for reasons such as longer study durations, irrelevant outcomes, supplement interventions, epidemiological studies, animal studies, any type of reviews, meta-analysis and protocols. Full texts were screened for the remaining eight studies. Finally, four studies, three full articles[30–32] and one conference proceeding[33], met the eligibility criteria and were included. These four papers yielded a reference list of eighty-five, which were scanned manually by LE and ESC, with no additional publications emerging for inclusion. The study identification process is presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram (Fig. 1).

Study characteristics

All included studies were RCT, two with a crossover[31,32] and two with a parallel design[30,33]. All intervened with a MDP and were carried out in non-Mediterranean countries, two Northern European[31,33] and two Australian[30,32]. The sample sizes ranged from 24[32] to 53[33]. Three of the studies included young females only, with mean ages of 21·1 (SD 3·3)[30], 22·3 (SD 3·7)[33] and 25·6 (SD 5·2)[32] years. The remaining study[31] included both males and females with metabolic syndrome traits with a participant mean age of 70 (SD 5) years. None of the four RCT reported any previous cognitive or mental health issues in the participants. Three had a study duration of 10 d, with one[31] examining the physiological response 4·5 h after the test meal. One study[31] implemented a MDP alone or with a physical activity intervention (30 min moderate walking).

In terms of the MDP intervention, in one crossover study[31], participants were provided with their test breakfast (4300 kJ) that consisted of ciabatta, smoked salmon, muesli, fruit and vegetables which was described as rich in unsaturated fatty acids,
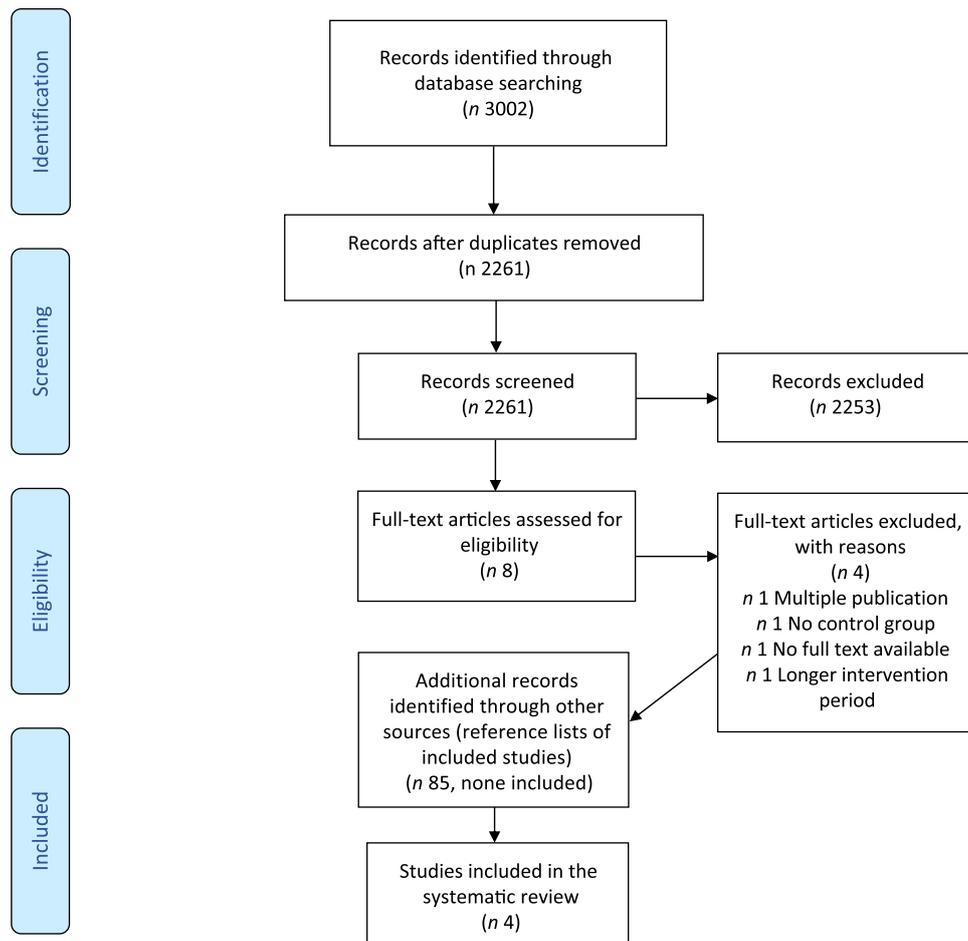

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

dietary fibre and antioxidative compounds. The remaining three studies did not provide the study foods but rather guided participants in following a MDP. De Vries *et al.*[33] did not provide any detail of the dietary instructions provided to participants. Lee *et al.*[32] requested participants in the MDP group to increase their intake of fruit, vegetables, oily fish, low-fat dairy products and nuts with a focus on healthy carbohydrates, fats and proteins, and to exclude meat, butter, margarine, caffeinated/energy drinks, added sugars and salts, alcohol, tobacco and illicit drugs during the study period. Besides, participants were also asked to consume freshly prepared foods and to avoid processed and packaged options where possible. Similarly, McMillan *et al.*[30] asked participants to increase their consumption of fruits, vegetables, oily fish, low-fat dairy products and nuts and to combine good sources of carbohydrates (less refined carbohydrates, whole grains, legumes, fruits and vegetables), fats and proteins. Additionally, they were instructed to abstain from red meat, refined sugars, refined flour, pre-packaged and processed foods, caffeinated products, soft drinks and condiments.

Regarding dietary assessment methods, food diaries were used over the 10-d study period in order to record the dietary intake in three of the studies[30,32,33]. The remaining study provided the foods, so no self-reported dietary assessment was required[31].

While three studies examined both mood and cognition as outcomes[30–32], one study assessed only mood[33]. The assessment methods for mood included the German version of Multidimensional Mood State Questionnaire[34] for subjective mood (good/bad mood; alertness/fatigue and ease/unease)[31], the Profiles of Mood States questionnaires[35] scoring the subscales tension/anxiety, fatigue/inertia, vigour/activity, confusion/bewilderment, anger/hostility, depression/rejection and the total mood disturbance score[30,32,33] and the Bond–Lader visual analogue scales[36] for the alertness, calmness and contentment[30,32,33]. For the assessment of cognition, the German version of the Frankfurt Attention Inventory 2 (test version A)[37] for attention[31] and the Computerised Mental Performance Assessment System[38] battery for a variety of cognitive domains were used[30,32] (Table 1).

Study quality

The study quality assessment showed that all included studies have a low risk of bias in the first three domains ((D1), bias arising from the randomisation process; (D2) bias due to deviations from intended interventions; (D3), bias due to missing outcome data), while the other two domains ((D4) bias in measurement of the outcome and (D5) bias in selection of the reported result) were assessed as having some concerns (Fig. 2).

Primary outcome measures

Cognition. According to the Computerised Mental Performance Assessment System results, increased correct responses (1·14, $F = 8.19$, $P = 0.01$) and decreased incorrect responses (–0·32, $F = 4.83$, $P = 0.04$) were seen in immediate word recall; reduced incorrect responses (–0·33, $F = 4.57$, $P = 0.046$) in delayed word recall were evident in the MDP group relative to the control,

Fig. 2. Risk of bias assessment results.

D1: bias arising from the randomisation process;
D2: bias due to deviations from intended interventions;
D3: bias due to missing outcome data;
D4: bias in measurement of the outcome;
D5: bias in selection of the reported result; D6: overall bias.

while correct responses significantly decreased in MDP treatment (–2·32, $F = 6.64$, $P = 0.02$) for the three-back task[32]. Reaction time increased for numeric working memory task in MDP by 2 % and decreased by 14 % in the control group ($F = 5.05$, $P = 0.04$); reduced for Corsi Blocks task by 14 % (–420) in MDP treatment and increased by 27 % (+837) in the control group ($F = 17.628$, $P < 0.001$)[30]. Whilst reaction times reduced in the word recognition task in both arms, it was not significant in the MDP (3 %, –29, $P = 0.574$) treatment and significant in the control group (20 %, –191, $P = 0.001$). The difference between the groups was significant ($F = 5.04$, $P = 0.035$)[30].

No overall significant effect of meal type in attention (as assessed by the Frankfurt Attention Inventory 2 method) was recorded. However, in the walking groups, a 1·4-fold increase was seen in the MDP group when compared with the WD, while this increase was 1·1-fold higher in the MDP relative to the WD in resting ($P = 0.045$ from iAUC data)[31].

Mood. Using the Profiles of Mood States questionnaire, vigour/activity ($P < 0.001$), tension/anxiety ($P = 0.001$), fatigue/inertia ($P = 0.003$), anger/hostility ($P = 0.014$), confusion/bewilderment ($P = 0.015$) and the total mood disturbance score (P value not stated) were significantly improved in the MDP arm compared with the control group[33]. Lowered confusion was observed by the MDP treatment (–1·19, $F = 6.87$, $P = 0.02$) with no other changes in the subscales of mood evident[32]. Following 10 d of MDP adherence, vigour rose by 18 % (3·67, $F = 11.25$, $P = 0.003$) in the MDP condition with no other dimensions of mood significantly affected[30].

Using the Bond–Lader scale, alertness and contentment were improved by MDP in all three studies used this scale. The results were as follows: alertness ($P = 0.003$) and contentment ($P = 0.001$)[33]; alertness (6·93, $F = 14.11$, $P < 0.01$) and contentment (5·35, $F = 6.49$, $P < 0.02$) scores[32]; and alertness (16·43 (about 30 %), $F = 22.23$, $P < 0.001$) and contentment (12·89 (about 20 %), $F = 16.634$, $P < 0.001$)[30]. No significant change was reported for calmness.

Using the Multidimensional Mood State Questionnaire test, no main effect of meal type interventions was observed for mood[31].

Secondary outcome measures

Two of the studies reported dietary adherence. In the Lee *et al.*'s study[32], all of the participants (*n* 24) an average MDP adherence of 94 % was evident which ranged from 80 % to 100 %. Similarly, in the McMillan *et al.*'s study[30], a mean MDP adherence of 93 % for meals (range 80–100 %) and 95 % for snacks (85–100 %) was reported.

No significant impact of a MDP meal *v.* WD meal on plasma cortisol levels was evident[31]. Only Lee *et al.* assessed the impact of intervention on blood pressure, blood flow velocity and arterial stiffness[32]. A significant decrease (−1·05, $F = 6·15$, $P = 0·02$) in augmentation pressure (mm Hg) was observed in the MDP condition relative to the control group.

Diekmann *et al.* assessed the desire to eat[31]. The overall hunger was not influenced by meal, while satiety was higher after MDP as compared with the WD ($P < 0·001$).

Body weight and BMI were tracked in two of the studies. Lee *et al.*[32] reported a significant weight loss in the MDP (−1·77 kg, $F = 10,81, P < 0·01$) group. McMillan *et al.*[30] observed no significant main effect of diet on body weight, BMI or waist circumference between the two groups.

Discussion

This is the first systematic review to report the short-term effects of a MDP on cognition and overall mental well-being. The findings suggest that a MDP has the potential to affect cognition and mood in as little as 10 d. The findings have also identified important research gaps notably; there are few reported studies and of the studies available most were conducted in young people, aged 18–38 years[30,32,33] and all conducted in individuals without cognitive or mental health complaints. In addition, there was a tendency to study females with only eighteen males in the 128 participants from the four studies. Therefore, the short-term effect of a MDP on mental health status in older adults, and in particular individuals who present with evidence of cognitive or mental health decline, is currently unknown.

Specific cognitive domains improved in all of the studies assessing the cognition, although the findings were not consistent[30–32]. Attention was significantly improved after the MDP in one study, with the authors speculating that this difference may be caused by the higher glucose content of the MDP (carbohydrate content of the meals: 133 g in MDP *v.* 93·7 g in WD) as the brain uses glucose as the primary source of energy[31]. Other studies reported improvements in immediate and delayed memory recall tasks, working memory and reaction times[32], and spatial working memory[30]. Consistent with these short-term effects, previous studies have reported longer-term (8 weeks) effects of a MDP enriched with dairy foods on processing speed in adults at above average CVD risk in the MedDairy study[39].

Mood dimensions, namely, alertness and contentment, were significantly and consistently improved by MDP in the short-term in all four studies. Vigour[30,33] and confusion[32,33] were also improved following the MDP. Adherence to a MDP has previously been shown to be associated with reduced risk of depression in elderly[40], and in the MedDairy study, a reduction in depression, tension, anger, confusion and total mood disturbance score was recorded following the 8-week dietary intervention period[39]. Furthermore, polyphenols intake, which are considered an important bioactive in the plant-based MDP, has shown to reduce depressive symptoms[41].

Previous short-term studies using other dietary intervention or health endpoints provide insight into the possible mechanistic basis for the effect of a MDP on mental health. Myette-Côté *et al.*[42] examined the effects of a low-fat, low glycaemic index diet, to a low carbohydrate diet or a low carbohydrate plus post-meal walking, in type 2 diabetes on glucose levels and inflammatory factors in a RCT comprising three 4-days interventions. While improved glycaemic control was evident in the low carbohydrate diet group, plasma monocyte-derived microparticles reduced significantly in the low-fat, low glycaemic index diet group which was similar to a MDP, suggesting that cerebral hypometabolism and inflammation which are features of cognitive disorders may be positively modulated by short-term dietary strategies. Attuquayefio *et al.*[43] reported a decrease in hippocampal-dependent learning and memory following a breakfast high in saturated fat, cholesterol and added sugar and low in protein relative to an isoenergetic healthy breakfast for 4 consecutive days, findings which were subsequently confirmed over a 1-week intervention period[44]. The hippocampus is a core brain area for cognitive functions such as learning and memory[45]. Besides, the hippocampus is involved in anxiety-related behaviours[46] and major depression[47]. This evidence suggests that the hippocampus function can be affected negatively by an unhealthy eating pattern in as short period as 4 d.

The hippocampus also produces high concentrations of brain-derived neurotrophic factor (BDNF) which is important in attention, cognition and total behaviour[48]. Decreased levels of BDNF have been linked to cognitive and mood disorders, and it has been identified as a therapeutic target in neurodegenerative and psychiatric impairments[49]. In PREDIMED study, a MDP raised BDNF levels over 3 years, whilst a MDP supplemented with nuts was linked to significant improvement in serum BDNF levels in individuals with depression[50]. However, the existing literature does not provide any insight into the short-term impacts of a MDP on BDNF levels.

Blood brain barrier is a dynamic selective interface between the brain and the bloodstream, in which dysregulations are associated with cognitive (including Alzheimer's disease) and psychiatric disorders[51]. Although selected dietary components have been shown to affect blood brain barrier function such as permeability in animal models[52] and the blood brain barrier is susceptible to be impairment by a WD[53], the impact of a MDP in short- or long-term mental health is currently unknown but should be a focus of investigation. Additionally, a reduction in cerebral blood flow is associated with cognitive dysfunction[54]. Lamport *et al.*[55] investigated the impacts of high flavanones on cognition and cerebral blood flow in young healthy participants in an acute RCT. A high flavanone citrus juice resulted in a 2-h increase in cerebral blood flow and better performance in one cognitive task (Digit Symbol Substitution) was observed in the experimental group. McManus *et al.*[56] examined the acute effects of EPA or DHA, found in oily fish, on arterial stiffness

in men at high risk of CVD. Four hours following to the test meal, vascular function was significantly improved by the DHA-rich oil. Besides, a MDP is known to chronically affect systematic vascular function[57].

The influences of the gut microbiota on cognition and overall mental well-being are well-recognised[58,59]. Therefore, nutritional strategies targeting the gut health may represent a meaningful strategy for delaying or even reversing neuropathology[60]. David *et al.*[61] demonstrated that the gut microbiota can be changed through both animal-based and plant-based diets in 5 d. Moreover, in a 1-year longitudinal study, the gut microbiota responded to daily changes in diet[62]. Hence, accumulating evidence suggests that the gut–brain axis could mediate the even short-term effects of a MDP on cognition and mental well-being.

The current review highlighted that all of the participants in the MDP treatments from the two studies tracking dietary adherence[30,32] reported high dietary adherence with no side effects. Besides, a MDP was linked to higher satiety in one study[31] and significant weight loss despite no energetic restriction in the another study[32]. Considering the fact that maintenance of healthy eating behaviours is not an easy task even in the short-term, this available evidence suggests that a MDP is an acceptable implementable approach even in non-Mediterranean countries.

The review has also highlighted a lack of consistency in how the MDP is applied. Despite the small number of included studies, none of them used the same dietary procedure, although the two Australian studies gave similar instructions to their participants[30,32]. Abdelhamid *et al.*[63] have previously reported the high inconsistencies in food and nutrient intake through when adopting a MDP. Davis *et al.*[64] also reported discrepancies in how the MDP was defined and the resulting nutrient intakes, with vegetable intakes, for example, ranged from 191 to 500 g/d in high MDP adherers. A greater standardisation in the definition of a MDP is needed in order to integrate data from difference sources and translate it in dietary recommendations focussed on improved short- and long-term health.

The main strength of the present paper is that it is the first systematic review to examine the short-term impact of a MDP on mood and cognition. Second, the database combination used ensured optimal coverage of the data[26,27] and has been shown by others to retrieve 95·9 % of available references[26]. Third, the review covers all available literature up to December 2020. As for limitations, the number of studies found was small; therefore, the conclusions are preliminary rather than robust. However, this limitation provided an opportunity to identify research gaps. The second limitation is the high heterogeneity in the dietary and mental health status assessments used. This methodological variability restricted making comparisons between studies.

In conclusion, the possible short-term beneficial impacts of a MDP on cognitive and mental health have been reviewed systematically for the first time. The results provide some initial evidence that short-term dietary interventions can confer health benefits which directly and/or indirectly improve cognitive and mental health. However, future studies are required to elucidate which cognitive and other mental health domains could be beneficially affected and what are the underlying physiological mechanism mediating the effects. Short-term strategies to improve cognition, mood and anxiety are not only of interest to improve quality of life and capabilities in those with existing mental health deficit but also in healthy individuals. The definition of the MDP in future studies should be carefully considered, with attention given to its population adoption taking into account social, geographical and cultural mediators of eating behaviours.

Acknowledgements

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114521002567

References

1. Nichols E, Szoeke CE, Vollset SE, *et al.* (2019) Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* **18**, 88–106.
2. Office for National Statistics (2020) Leading causes of death, UK: 2001 to 2018 - Office for National Statistics. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/articles/leadingcausesofdeathuk/2001to2018#toc (accessed January 2021).
3. Prince M, Wimo A, Guerchet M, *et al.* (2015) The global impact of dementia. World Alzheimer Report 2015, The Global Impact of Dementia: an analysis of prevalence, incidence, cost and trends. https://www.alzint.org/u/WorldAlzheimerReport2015.pdf (accessed January 2021).
4. Petersen RC (2016) Mild cognitive impairment. *Continuum: Lifelong Learn Neurol* **22**, 404.
5. Jessen F, Amariglio RE, Buckley RF, *et al.* (2020) The characterisation of subjective cognitive decline. *Lancet Neurol* **19**, 271–278.
6. Jessen F, Amariglio RE, van Boxtel M, *et al.* (2014) A conceptual framework for research on subjective cognitive decline in

preclinical Alzheimer's disease. *Alzheimer's Dementia* **10**, 844–852.

7. WHO (2017) Depression and Other Common Mental Disorders, Global Health Estimates. https://www.who.int/publications/i/item/depression-global-health-estimates (accessed January 2021).

8. James SL, Abate D, Abate KH, *et al.* (2018) Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* **392**, 1789–1858.

9. Livingston G, Sommerlad A, Orgeta V, *et al.* (2017) Dementia prevention, intervention, and care. *Lancet* **390**, 2673–2734.

10. Jennings A, Cunnane SC & Minihane AM (2020) Can nutrition support healthy cognitive ageing and reduce dementia risk? *BMJ* **369**, m2269.

11. Willett WC, Sacks F, Trichopoulou A, *et al.* (1995) Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr* **61**, 1402S–1406S.

12. Visioli F, Franco M, Toledo E, *et al.* (2018) Olive oil and prevention of chronic diseases: Summary of an International conference. *Nutr Metab Cardiovasc Dis* **28**, 649–656.

13. Gorzynik-Debicka M, Przychodzen P, Cappello F, *et al.* (2018) Potential health benefits of olive oil and plant polyphenols. *Int J Mol Sci* **19**, 686.

14. Kromhout D, Menotti A, Bloemberg B, *et al.* (1995) Dietary saturated and transFatty acids and cholesterol and 25-year mortality from coronary heart disease: the seven countries study. *Preventative Med* **24**, 308–315.

15. Bendall CL, Mayr HL, Opie RS, *et al.* (2018) Central obesity and the Mediterranean diet: a systematic review of intervention trials. *Crit Rev Food Sci Nutr* **58**, 3070–3084.

16. Kastorini C-M, Milionis Haralampos J, Esposito K, *et al.* (2011) The effect of mediterranean diet on metabolic syndrome and its components. *J Am Coll Cardiol* **57**, 1299–1313.

17. de Lorgeril M, Salen P, Martin J-L, *et al.* (1999) Mediterranean Diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction. *Circulation* **99**, 779–785.

18. Shannon OM, Stephan BCM, Granic A, *et al.* (2019) Mediterranean diet adherence and cognitive function in older UK adults: the European Prospective Investigation into Cancer and Nutrition-Norfolk (EPIC-Norfolk) Study. *Am J Clin Nutr* **110**, 938–948.

19. Martínez-González MÁ, Corella D, Salas-Salvadó J, *et al.* (2012) Cohort profile: design and methods of the PREDIMED study. *Int J Epidemiol* **41**, 377–385.

20. Martinez-Lapiscina EH, Clavero P, Toledo E, *et al.* (2013) Mediterranean diet improves cognition: the PREDIMED-NAVARRA randomised trial. *J Neurol Neurosurg Psychiatr* **84**, 1318–1325.

21. Sanchez-Villegas A, Martinez-Gonzalez MA, Estruch R, *et al.* (2013) Mediterranean dietary pattern and depression: the PREDIMED randomized trial. *BMC Med* **11**, 208.

22. Wu L & Sun DL (2017) Adherence to Mediterranean diet and risk of developing cognitive disorders: an updated systematic review and meta-analysis of prospective cohort studies. *Sci Rep* **7**, 1–9.

23. Shafiei F, Salari-Moghaddam A, Larijani B, *et al.* (2019) Adherence to the Mediterranean diet and risk of depression: a systematic review and updated meta-analysis of observational studies. *Nutr Rev* **77**, 230–239.

24. Liberati A, Altman DG, Tetzlaff J, *et al.* (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* **62**, e1–e34.

25. Esgunoglu L, Jennings A, Murphy K, *et al.* (2021) Short-Term Effects of a Mediterranean-Style Dietary Pattern and Olive Oil on Cognition, Mood and Mental Wellbeing: a Systematic Review of Clinical Trials. PROSPERO: University of York. https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=221085 (accessed February 2021).

26. Bramer WM, Rethlefsen ML, Kleijnen J, *et al.* (2017) Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. *Syst Rev* **6**, 245.

27. Gusenbauer M & Haddaway NR (2020) Which academic search systems are suitable for systematic reviews or meta-analyses? Evaluating retrieval qualities of Google Scholar, PubMed, and 26 other resources. *Res Synth Methods* **11**, 181–217.

28. Dictionary OE Cognition LEXICO powered by Oxford. COGNITION | Definition of COGNITION by Oxford Dictionary. https://www.lexico.com/definition/cognition (accessed January 2021).

29. Sterne JAC, Savović J, Page MJ, *et al.* (2019) RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* **366**, l4898.

30. McMillan L, Owen L, Kras M, *et al.* (2011) Behavioural effects of a 10-day Mediterranean diet. Results from a pilot study evaluating mood and cognitive performance. *Appetite* **56**, 143–147.

31. Diekmann C, Wagner M, Huber H, *et al.* (2019) Acute impact of dietary pattern and walking on postprandial attention, mood, and satiety in older adults: a randomized crossover trial. *Nutrients* **11**, 2294.

32. Lee J, Pase M, Pipingas A, *et al.* (2015) Switching to a 10-day Mediterranean-style diet improves mood and cardiovascular function in a controlled crossover study. *Nutrition* **31**, 647–652.

33. De Vries E, Van Schrojenstein Lantman M, Hoebregts V, *et al.* (2017) Mediterranean diet and mood. *Eur Neuropsychopharmacol* **27**, S879–S880.

34. Steyer R, Schwenkmezger P, Notz P, *et al.* (1994) Testtheoretische Analysen des Mehrdimensionalen Befindlichkeitsfragebogen (MDBF) (Testtheoretical analyses of the Multidimensional Mood Questionnaire (MDMQ) Diagnostica. Testtheoretische Analysen des Mehrdimensionalen Befindlichkeitsfragebogen (MDBF). – PsycNET. https://psycnet.apa.org/record/1995-86418-001 (accessed May 2021).

35. McNair D, Lorr M & Droppleman L (1971) Manual for the Profile of Mood States (POMS). San Diego: Educational and Industrial Testing Service. https://www.scirp.org/reference/ReferencesPapers.aspx?ReferenceID=1822161 (accessed May 2021).

36. Bond A & Lader M (1974) The use of analogue scales in rating subjective feelings. *Br J Med Psychol* **47**, 211–218.

37. Petermann F (2011) Frankfurter Aufmerksamkeits-Inventar 2 (FAIR-2) (Frankfurt Attention Inventory). *Z für Psychiatrie, Psychologie Psychotherapie* **59**, 325–326.

38. Scholey A, Ossoukhova A, Owen L, *et al.* (2010) Effects of American ginseng (Panax quinquefolius) on neurocognitive function: an acute, randomised, double-blind, placebo-controlled, crossover study. *Psychopharmacol* **212**, 345–356.

39. Wade AT, Davis CR, Dyer KA, *et al.* (2020) A Mediterranean diet supplemented with dairy foods improves mood and processing speed in an Australian sample: results from the MedDairy randomized controlled trial. *Nutr Neurosci* **23**, 646–658.

40. Masana MF, Haro JM, Mariolis A, *et al.* (2018) Mediterranean diet and depression among older individuals: the multinational MEDIS study. *Exp Gerontol* **110**, 67–72.

41. Bayes J, Schloss J & Sibbritt D (2020) Effects of polyphenols in a Mediterranean diet on symptoms of depression: a systematic literature review. *Adv Nutr* **11**, 602–615.

42. Myette-Côté É, Durrer C, Neudorf H, *et al.* (2018) The effect of a short-term low-carbohydrate, high-fat diet with or without post-meal walks on glycemic control and inflammation in type 2

diabetes: a randomized trial. *Am J Physiol Regul Integr Comp Physiol* **315**, R1210–R1219.

43. Attuquayefio T, Stevenson RJ, Oaten MJ, *et al.* (2017) A four-day Western-style dietary intervention causes reductions in hippocampal-dependent learning and memory and interoceptive sensitivity. *PLoS One* **12**, e0172645.

44. Stevenson RJ, Francis HM, Attuquayefio T, *et al.* (2020) Hippocampal-dependent appetitive control is impaired by experimental exposure to a Western-style diet. *Royal Soc Open Sci* **7**, 191338.

45. Driscoll I, Hamilton DA, Petropoulos H, *et al.* (2003) The aging hippocampus: cognitive, biochemical and structural findings. *Cereb Cortex* **13**, 1344–1351.

46. Bannerman DM, Rawlins JNP, McHugh SB, *et al.* (2004) Regional dissociations within the hippocampus – memory and anxiety. *Neurosci Biobehav Rev* **28**, 273–283.

47. MacQueen GM, Campbell S, McEwen BS, *et al.* (2003) Course of illness, hippocampal function, and hippocampal volume in major depression. *Proc Natl Acad Sci* **100**, 1387.

48. Yeom C-W, Park Y-J, Choi S-W, *et al.* (2016) Association of peripheral BDNF level with cognition, attention and behavior in preschool children. *Child Adolesc Psychiatr Ment Health* **10**, 10.

49. Teixeira AL, Barbosa IG, Diniz BS, *et al.* (2010) Circulating levels of brain-derived neurotrophic factor: correlation with mood, cognition and motor function. *Biomarkers Med* **4**, 871–887.

50. Sanchez-Villegas A, Galbete C, Martinez-Gonzalez MA, *et al.* (2011) The effect of the Mediterranean diet on plasma brain-derived neurotrophic factor (BDNF) levels: the PREDIMED-NAVARRA randomized trial. *Nutr Neurosci* **14**, 195–201.

51. Kealy J, Greene C & Campbell M (2020) Blood-brain barrier regulation in psychiatric disorders. *Neurosci Letter* **726**, 133664.

52. Youdim KA, Shukitt-Hale B & Joseph JA (2004) Flavonoids and the brain: interactions at the blood–brain barrier and their physiological effects on the central nervous system. *Free Radical Biol Med* **37**, 1683–1693.

53. Hsu TM & Kanoski SE (2014) Blood-brain barrier disruption: mechanistic links between Western diet consumption and dementia. *Front Aging Neurosci* **6**, 88.

54. Mattsson N, Tosun D, Insel PS, *et al.* (2014) Association of brain amyloid-β with cerebral perfusion and structure in Alzheimer's disease and mild cognitive impairment. *Brain* **137**, 1550–1561.

55. Lamport DJ, Pal D, Macready AL, *et al.* (2016) The effects of flavanone-rich citrus juice on cognitive function and cerebral blood flow: an acute, randomised, placebo-controlled cross-over trial in healthy, young adults. *Br J Nutr* **116**, 2160–2168.

56. McManus S, Tejera N, Awwad K, *et al.* (2016) Differential effects of EPA versus DHA on postprandial vascular function and the plasma oxylipin profile in men. *J Lipid Res* **57**, 1720–1727.

57. Shannon OM, Mendes I, Köchl C, *et al.* (2020) Mediterranean diet increases endothelial function in adults: a systematic review and meta-analysis of randomized controlled trials. *J Nutr* **150**, 1151–1159.

58. Foster JA & McVey Neufeld K-A (2013) Gut–brain axis: how the microbiome influences anxiety and depression. *Trends Neurosci* **36**, 305–312.

59. Proctor C, Thiennimitr P, Chattipakorn N, *et al.* (2017) Diet, gut microbiota and cognition. *Metab Brain Dis* **32**, 1–17.

60. Bischoff SC (2016) Microbiota and aging. *Curr Opin Clin Nutr Metab Care* **19**, 26–30.

61. David LA, Maurice CF, Carmody RN, *et al.* (2014) Diet rapidly and reproducibly alters the human gut microbiome. *Nature* **505**, 559–563.

62. David LA, Materna AC, Friedman J, *et al.* (2014) Host lifestyle affects human microbiota on daily timescales. *Genome Biol* **15**, R89.

63. Abdelhamid A, Jennings A, Hayhoe RPG, *et al.* (2020) High variability of food and nutrient intake exists across the Mediterranean Dietary pattern – a systematic review. *Food Sci Nutr* **8**, 4907–4918.

64. Davis C, Bryan J, Hodgson J, *et al.* (2015) Definition of the Mediterranean diet; a literature review. *Nutrients* **7**, 9139–9153.