Review

Is the Mediterranean diet a feasible approach to preserving cognitive function and reducing risk of dementia for older adults in Western countries? New insights and future directions

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\textbf{ABSTRACT}

The rise in the ageing population has resulted in increased incident rates of cognitive impairment and dementia. The subsequent financial and societal burden placed on an already strained public health care system is of increasing concern. Evidence from recent studies has revealed modification of lifestyle and dietary behaviours is, at present, the best means of prevention. Some of the most important findings, in relation to the Mediterranean diet (MedDiet) and the contemporary Western diet, and potential molecular mechanisms underlining the effects of these two diets on age-related cognitive function, are discussed in this review. A major aim of this review was to discuss whether or not a MedDiet intervention would be a feasible preventative approach against cognitive decline for older adults living in Western countries. Critical appraisal of the literature does somewhat support this idea. Demonstrated evidence highlights the MedDiet as a potential strategy to reduce cognitive decline in older age, and suggests the Western diet may play a role in the aetiology of cognitive decline. However, strong intrinsic Western socio-cultural values, traditions and norms may impede on the feasibility of this notion.

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1. Introduction

Cognitive ageing is a major concern to older adults in industrialised Western countries. Two national health surveys taken in the United States of America (The PARADISE/Research!America Health, 2006–2007) and in Australia (Pfizer Australia HEALTH REPORT, 2005) revealed that for adults of all ages, losing one's mental capacity was reported as one of the greatest fears of growing older (Vandenbeld et al., 2012). This finding is understandable given the debilitating consequences that accompany irreversible loss of cognitive function, such as diminished quality of life, loss of autonomy and independence, increased health care costs, and subsequent burdens to family members (Sloane et al., 2002).

Furthermore, advancing age itself is the foremost risk factor for cognitive decline and dementia (Blasko et al., 2004). Indeed, the rising ageing population has contributed to the highest prevalence rates of dementia seen throughout history. At present, the number of individuals living with Alzheimer's disease (AD), the most common type of dementia among the elderly, is estimated at around 47.5 million worldwide (WHO, 2015). With 9.5 million new cases of dementia emerging each year, this concerning trend is predicted to rise even higher in the future (ADI, 2015). Extra health care costs, aged care facilities, medical and counselling support services will be needed to facilitate the escalating number of sufferers and subsequent dependency. In order to prevent a major public health crisis in the near future, sustainable diet and lifestyle strategies that minimise such anticipated future burden, promote healthy cognitive ageing, and enhance the overall quality of life for older adults are urgently needed.

Over the last decade, researchers have begun scientific exploration of how whole dietary patterns influence the brain, rather than foods and nutrients in isolation. This research has advanced our knowledge and understanding of the synergistic effects of food combinations on human neurobiology, and how this relates to subsequent cognitive function in older age (Kant, 2004; Sofi et al., 2010). The combined, interrelated actions of multiple food components within whole dietary patterns are thought to bring about unique synergistic, additive, and interactive effects in the brain (Gómez-Pinilla, 2008). Such multifactorial effects are postulated to influence neuronal and cell signalling pathways at a molecular level in the brain, which, in turn, are known to play a crucial role in the development and maintenance of cognitive function (Jacobs et al., 2009).

Interestingly, various dietary patterns with differing food and nutrient compositions, are thought to elicit different manifestations of these effects on the ageing brain. For example, among older adults, high saturated fat and simple carbohydrate based dietary patterns (e.g. components of the Western diet) are suggested to contribute to neurodegeneration, leading to subsequent impairment in cognitive function (Patterson et al., 2012). In contrast, healthier food patterns, such as the traditional Mediterranean diet (MedDiet) are postulated to possess neuroprotective properties, thus supporting preservation of cognitive ability in older age (Scarmeas et al., 2009; Simopoulos, 2001). Indeed, the most compelling argument for optimal age-related cognitive health in the literature at present expresses the avoidance of high-saturated and simple carbohydrate dietary patterns and the adoption of a healthy eating model, such as the MedDiet (Lourida et al., 2013; Martínez-Lapiscina et al., 2013; Solfrizzi et al., 2011).

In line with this reasoning, two important questions relating specifically to older adults living in Western industrialised countries (e.g. Australia, United States, Canada, New Zealand) should be considered. First, does the current body of evidence relating to the traditional MedDiet infer a level of benefit for age-related cognitive function that warrants its use as a preventative strategy for older adults in Western countries? Second, is it feasible to encourage older adults with Western habitual dietary habits to adopt a traditional MedDiet pattern, for greater age-related cognitive health? Answers to these questions will be important for older adults who are concerned about the development of cognitive decline and dementia as well as the implications for the wider public health system. Future Governments and medical practitioners looking for novel ways to reduce the burden of dementia may be interested in translating a synthesis of empirical evidence into new policies and practices that can be used to promote specific dietary recommendations for age-related cognitive health.

In the present review these questions are considered within the context of current empirical evidence. From this knowledge base, a clearer understanding of whether a MedDiet intervention may be a valid (i.e. the diet demonstrates a credible effect) and feasible (i.e. adherence to the diet is genuinely possible in the real-world) approach to greater cognitive function for older adults in Western populations is presented. Due to the wealth of available research in the area, an exhaustive systematic review was not feasible. Rather, a coherent overview of evidence from a selective framework of principal studies were examined and summarised to enable critical evaluation of the following five topics: 1. the association between the MedDiet pattern and age-related cognitive function; 2. potential mechanisms underlying the effects of the traditional MedDiet on age-related cognitive function; 3. the association between the Western dietary pattern and age-related cognitive function; 4. potential mechanisms underlying the effects of the contemporary Western diet on age-related cognitive function; and 5. the feasibility of a MedDiet intervention in industrialised Western cultures (including socio-cultural elements of both the MedDiet and the Western diet, palatability, availability, convenience and cost). In addition, synthesis of these topics is presented within a biopsychosocial model.

A search was undertaken of the following electronic databases: EMBASE via the Ovid interface and PubMed via the PMC interface, to identify salient studies in the five areas of interest mentioned above, which could most adequately assist in objectively evaluating the topic of interest. The following key search terms were used: “Mediterranean diet”, “Western diet”, “saturated fat”, “refine sugars”, “cognition”, “cognitive function”, “cognitive performance”, “dementia”, “Alzheimer”, and “ageing”. Only English language peer reviewed publications were searched, and there was no restriction on study design. The focus for this review was to obtain the highest level of evidence possible. Thus, foremost randomised controlled interventions, cross-sectional and prospective studies were considered, and letters, opinions, editorials, abstracts, dissertations and review papers were excluded.

2. The traditional Mediterranean dietary pattern

2.1. The association between the Mediterranean dietary pattern and age-related cognitive function

The traditional MedDiet originated from Crete, Greece among populations bordering the Mediterranean sea in the south of Europe. The MedDiet was first described in the Seven Countries Study in the 1950s–1960s (Feinleib, 1981), and characterised by high intakes of vegetables, fruits, olive oil, legumes, fish, whole grain cereals, nuts and seeds; moderate red wine consumption; and low consumption of processed foods, dairy products, red meat and vegetable oils (Willett et al., 1995).

Among reviewed studies examining the association between MedDiet intake and pathological cognitive function (i.e. MCI, AD, dementia), there was a general consensus that increased MedDiet adherence lead to reduced risk of MCI (Gardener et al., 2012; Robert et al., 2010; Scarmeas et al., 2009), AD (Gardener et al,
### Table 1
Principal empirical studies investigating the association between the Mediterranean dietary pattern and age-related cognitive function.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study population</th>
<th>Study design follow-up</th>
<th>Sample size</th>
<th>Mean age (SD)</th>
<th>Cognitive outcomes</th>
<th>Efficacy</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cherbuin and Anstey (2012)</td>
<td>Older adults Australia</td>
<td>Longitudinal (4 years)</td>
<td>1,528</td>
<td>62.5 (1.5)</td>
<td>Age-related cognitive decline, –</td>
<td>–</td>
<td>In a large healthy Australian older adult sample, greater adherence to a MeDi pattern was not found to be protective of age-related cognitive decline over a 4 year duration.</td>
</tr>
<tr>
<td>Corley et al. (2013)</td>
<td>Older adults Scotland</td>
<td>Cross-sectional (no follow-up)</td>
<td>882</td>
<td>70.0 (0.8)</td>
<td>Age-related cognitive performance –</td>
<td>–</td>
<td>Among older adults from the Lothian Birth Cohort (1936) study, the statistical models showed no significant link between adherence to a Mediterranean-style pattern and benefit on general cognitive function in older age, (βp2 = 0.000; p = 0.96).</td>
</tr>
<tr>
<td>Feart et al. (2009)</td>
<td>Older adults France</td>
<td>Longitudinal (5 years)</td>
<td>1,410</td>
<td>75.9 (4.9)</td>
<td>Age-related cognitive decline dementia risk, ▲ GCP – D</td>
<td>▲ GCP – D</td>
<td>After adjustments, higher adherence to a MeDi pattern was associated with significantly slower decline in MMSE performance (i.e. global cognitive function); (β) = –0.006; 95% (CI), –0.01 to –0.003, p = .04. However, not for risk of incident dementia, HR = 1.12; 95% (CI), 0.60 to 2.10; p = .72.</td>
</tr>
<tr>
<td>Gardener et al. (2012)</td>
<td>Older adults Australia</td>
<td>Cross-sectional (1.5 years)</td>
<td>723</td>
<td>69.9 (6.9)</td>
<td>Age-related cognitive performance, MCI risk, AD risk ▲</td>
<td>▲</td>
<td>In a large Australian elderly cohort a significant difference was observed in adherence to a MeDi diet between healthy control (HC) subjects and MCI subjects and also between HC and AD subjects on global cognitive function, each additional unit of MeDi adherence was associated with a 13–19% lower odds of MCI, and 19–26% lower odds of AD.</td>
</tr>
<tr>
<td>Gu et al. (2010)</td>
<td>Older adults USA</td>
<td>Cross-sectional (3.8 years)</td>
<td>1,219</td>
<td>76.3 (6.3)</td>
<td>Age-related cognitive performance, AD risk ▲</td>
<td>▲</td>
<td>Higher adherence to a MeDi pattern was associated with a significantly lower risk for AD compared to those in the lowest tertile of adherence to a MeDi, those in the highest tertile group had a 34% less risk of developing AD (p-trend = 0.04).</td>
</tr>
<tr>
<td>Kesse-Guyot et al. (2013)</td>
<td>Older adults France</td>
<td>Longitudinal (13 years)</td>
<td>3,083</td>
<td>65.4 (4.6)</td>
<td>Age-related cognitive performance –</td>
<td>–</td>
<td>Among a French population of older adults, midlife adherence to a MedDiet pattern was not associated with global cognitive performance assessed 13 years later, after major confounders were accounted for, SMD = –0.17; 95% (CI), –0.96 to 0.63, p-trend = 0.12.</td>
</tr>
<tr>
<td>Martinez-Lapiscina et al. (2013)</td>
<td>Older adults Spain</td>
<td>RCT (6.5 years)</td>
<td>522</td>
<td>67.4 (5.6)</td>
<td>Age-related cognitive performance, incidence of MCI and dementia ▲</td>
<td>▲</td>
<td>Older Spanish adults randomly allocated to the MedDiet + EVOO group showed significantly higher mean MMSE and CDT scores compared to the control group, adjusted differences: +0.57; 95% (CI), +0.11 to +1.03, p = 0.015 for MMSE and +0.33; 95% (CI), +0.03 to +0.67, p = 0.048 for CDT.</td>
</tr>
</tbody>
</table>
Table 1 (Continued)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Efficacy</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samieri et al. (2013a)</td>
<td>Older adults USA</td>
<td>Longitudinal (4 years)</td>
<td>6,174</td>
<td>72.0 (4.1)</td>
<td>Age-related cognitive decline &amp; performance</td>
<td>–</td>
<td>After multivariable adjustments, no significant associations were observed between aMedi adherence and cognitive performance, or cognitive decline overtime, MMD = 0.02; 95% (CI), -0.03–0.06.</td>
</tr>
<tr>
<td>Samieri et al. (2013b)</td>
<td>Older adults USA</td>
<td>Longitudinal (6 years)</td>
<td>16,058</td>
<td>74.3 (2.3)</td>
<td>Age-related cognitive decline, cognitive performance</td>
<td>–</td>
<td>In the first analyses of cognitive change, the A-Medi was not associated with change over time in any of the observed cognitive outcomes, including overall, global cognitive function, MMD = –0.001; 95% (CI), –0.02–0.07, p-trend = 0.44. In the second analyses, higher long-term A-Medi adherence was found linearly related to higher performance status on all cognitive outcomes, global cognition, MMD = 0.05; 95% (CI), 0.01–0.08, p-trend = 0.002, and verbal memory, MMD = 0.06; 95% (CI), 0.03–0.10, p-trend = 0.001.</td>
</tr>
<tr>
<td>Scarmeas et al. (2006)</td>
<td>Older adults USA</td>
<td>Longitudinal (4 years)</td>
<td>2,258</td>
<td>76.5 (6.3)</td>
<td>Age-related cognitive decline, AD risk</td>
<td>▲</td>
<td>Higher adherence to a MedDiet pattern was associated with a significantly lower risk for AD (HR = 0.91; 95% (CI), 0.83–0.98, p = 0.015) and also slower cognitive decline, (β = 0.003; p = 0.047) with 0.3% less decline per year for each additional unit of adherence to the MedDiet compared to the lowest tertile (HR = 0.72; 95% (CI), 0.52–1.00; p = .05), and a 48% less risk of developing AD, HR = 0.52; 95% (CI), 0.30–0.91; p = .02 of developing AD.</td>
</tr>
<tr>
<td>Scarmeas et al. (2009)</td>
<td>Older adults USA</td>
<td>Longitudinal (4.5 years)</td>
<td>1,393</td>
<td>76.9 (6.5)</td>
<td>Age-related MCI risk, conversion to AD</td>
<td>▲</td>
<td>Older adult subjects from the USA in the highest MedDiet adherence tertile had a 28% less risk of developing MCI compared to those in the lowest tertile (HR = 0.72; 95% (CI), 0.52–1.00; p = .05), and a 48% less risk of developing AD, HR = 0.52; 95% (CI), 0.30–0.91; p = .02 of developing AD.</td>
</tr>
<tr>
<td>Roberts et al. (2010)</td>
<td>Older adults USA</td>
<td>Longitudinal (7.2 years)</td>
<td>1,233</td>
<td>81.5 (2.5)</td>
<td>Incidence of MCI and dementia</td>
<td>▲</td>
<td>In a large American elderly sample, higher adherence to a MedDiet pattern was associated with a reduced risk of incident MCI or dementia, HR = 0.75; 95% (CI), 0.46–1.21, p = 0.24.</td>
</tr>
<tr>
<td>Tangney et al. (2011)</td>
<td>Older adults USA</td>
<td>Longitudinal (7.6 years)</td>
<td>3790</td>
<td>75.4 (6.2)</td>
<td>Age-related cognitive decline</td>
<td>▲</td>
<td>Higher MedDiet adherence scores were significantly associated with slower rates of cognitive decline after adjustments, (β = 0.0014 per 1-point increase, SEE = 0.0004, p = 0.0004)</td>
</tr>
<tr>
<td>Valls-Pedret et al. (2015)</td>
<td>Older adults Spain</td>
<td>RCT (4.1 years)</td>
<td>447</td>
<td>66.9 (not located)</td>
<td>Age-related cognitive performance and, cognitive decline</td>
<td>▲</td>
<td>Older Spanish adults randomly allocated to the MedDiet + EVOO group showed significantly higher RAVLT (p = 0.049) and Color Trail Test 2 (p = 0.04) scores compared to the control group. Mean z-scores of change for adjusted cognitive composites revealed above baseline the MedDiet + EVOO group were 0.04 (−0.09–0.18) for memory, 0.23 (0.03 to 0.43; p = 0.003 vs. controls) for frontal cognition, and 0.05 (−0.11–0.21; p = .005 vs. controls) for global. For the MedDiet + mixed nuts group; 0.09 (−0.05 to 0.23; p = .04 vs. controls) for memory, 0.03 (−0.25–0.31) for global cognition, and −0.05 (−0.27–0.18) for global.</td>
</tr>
</tbody>
</table>

Abbreviations: AD = Alzheimer’s disease; aMedi; Medi; MSDPS = Mediterranean style dietary pattern; MedDiet + EVOO = Mediterranean dietary pattern plus extra virgin olive oil; MedDiet + Nuts = Mediterranean dietary pattern plus unprocessed mixed nuts (walnuts, almonds and hazelnuts); CDT = Clock Drawing Test; CI = confidence interval; β = standardized coefficient; D = dementia; GCP = global cognitive performance; HR = hazard ratio; MCI = mild cognitive impairment; MMD = multivariable mean difference in standard units; MMSE = Mini Mental State Examination; η² = partial eta square; p = value; statistical significance less than 0.05; SEE = standard error of estimate; SMD = standardised mean difference. Efficacy values: ▲ = MedDiet improved outcomes, – MedDiet had no effect, ▼ = MedDiet had a detrimental effect on outcomes.
of cognitive (Martínez-Lapiscina et al., 2013; Singh et al., 2014; Sofi et al., 2010), lending further support to the postulated benefit of the MedDiet on reducing risk of developing clinical neurodegenerative disease in older age. However, as noted by Sofi et al. (2010), most of these studies were performed on the same cohort of participants. Thus, despite extended follow-up time and the use of different statistical analyses, it is not clear whether or not the results can be generalised beyond the study populations.

In comparison to studies investigating clinical older adult populations, less consistent findings have come from studies investigating healthy older adult populations. Among the principal papers reviewed here, a number of studies found increasing adherence to a MedDiet pattern were significantly associated with improvement on a range of cognitive outcomes, independent of cardiovascular risk factors, including: higher global cognitive performance (Feart et al., 2009; Gardener et al., 2012; Gu et al., 2010; Psaltopoulou et al., 2008; Samieri et al., 2013b), higher verbal memory (Samieri et al., 2013b) and higher verbal episodic memory performance in participants who did not develop dementia over a five year study duration (Feart et al., 2009). Other studies have documented higher adherence to a MedDiet pattern significantly related to cognitive decline over time (Scarmeas et al., 2006; Tangney et al., 2011). In contrast, evidence from a number of other prior studies have indicated that higher adherence to a MedDiet pattern was not associated with age-related cognitive performance (Corley et al., 2013; Kesse-Guyot et al., 2013; Samieri et al., 2013a), or reduce the rate of cognitive decline overtime (Cherbuin and Anstey, 2012; Samieri et al., 2013a; Samieri et al., 2013b) among healthy older adult populations (see Table 1).

An interesting outcome of these studies was that a positively significant relationship between MedDiet adherence and age-related cognitive outcomes was most consistently found in studies that examined pathological brain ageing (dementia and AD risk, MCI conversion to AD) compared with healthy cognitive ageing. Thus, it may be that the timeframe in which the MedDiet offers the most beneficial effect in older age is in fact within the prodromal phase of cognitive function (i.e. the preceding phase of early neurodegenerative symptomatology before the fully manifested clinical disease of dementia emerges) (Welsh-Bohmer, 2008). The relevance of this finding, if validated by future studies, could be very useful in directing preventative action against pathological cognitive function in older age. Indeed, it has been proposed that an intervention with the capability of delaying the onset of AD by only five years would reduce the expected prevalence of AD by 50% (1.15 million patients) in the United States after ten years (Brookmeyer et al., 1998).

To date, there has only been two reported randomised controlled trials (RCT) that have investigated the effects of a MedDiet on age-related cognitive function. In a 5 year RCT conducted in Spain, Martínez-Lapiscina et al. (2013) found among S22 elderly participants at high risk of cardiovascular disease, after a mean follow-up of 6.5 years, global cognitive performance scores, as indicated by the Mini-Mental State Examination (MMSE) (Folstein et al., 1975) and the Clock Drawing Test (CDT) (del Ser Quijano et al., 2004) were significantly higher for participants randomised to a MedDiet pattern (supplemented with either extra-virgin olive oil (EVOO) or mixed nuts) versus the low-fat diet control group.

Similarly, in another parallel-group RCT conducted in Spain (Valls-Pedret et al., 2015), 447 older adults at high cardiovascular risk were randomly allocated to one of three groups: a MedDiet intervention supplemented with either extra-virgin olive oil (EVOO): a MedDiet intervention supplemented with mixed nuts, or a control diet (advised to reduce dietary fat). All participants underwent a series of cognitive tests approximately 4.1 years after the intervention. Results indicated that participants allocated to the MedDiet + EVOO scored significantly higher on the Rey Auditory Verbal Learning Test (RAVLT) (Schmidt, 1996), and the Colour Trail Test part 2 (D’Elia et al., 1996) compared with the control group. No significant between-group differences were observed for the MedDiet + nuts group versus the control group. Composite scores for memory, frontal (attention and executive functions), and global revealed the MedDiet + EVOO group as well as the MedDiet + mixed nuts group showed significant respective changes from baseline compared to the control group (see Table 1).

Taken together, these findings provide preliminary evidence for the hypothesised benefit of a MedDiet intervention on age-related cognitive function. Additionally, the results of these two RCTs indicate that while the control groups maintained a relatively healthy, low-fat diet for the duration of the trial, they still performed significantly worse than those older adults who maintained a MedDiet. As such, while it seems rational to assume that the positive results documented in prior studies relating to the MedDiet may equally be derived from simply the absence of unhealthy foods, the findings of these RCTs proposes otherwise. The participants allocated to the “low-fat” diet groups were also adhering to an elimination-type diet (no high-fat unhealthy foods). Hence, it is plausible that the specific foods and nutrients contained within a MedDiet pattern, when synergistically combined, are more powerful on the ageing brain than merely consuming a low-fat diet. This lends further query into the underlying mechanisms of the MedDiet, and what it is exactly about the specific foods and nutrients within this diet that produces such neuroprotective benefits, and how it differs from other diets.

2.2. Underlying mechanisms of the Mediterranean dietary pattern on age-related cognition

While adherence to the MedDiet has been shown to improve age-related cognitive outcomes in a number of recent studies, one fundamental question remains poorly understood, and relatively unexplored: “how exactly does a traditional MedDiet pattern exert such postulated effects? This type of question relates to the potential underlying mechanism of the whole MedDiet pattern on age-related cognitive outcomes (Glennan, 1996). Although no such mechanism has been clearly proposed, examining the potential role of various dietary and biological mechanisms on mitochondrial health and neuronal and cell signalling pathways, may help explain the molecular basis of the effect of MedDiet intake on age-related cognitive function. Currently, the most compelling theory relates to the interactions of multiple nutrient-rich food components in the diet. It is thought that such interactions may exert powerful synergism, which, in turn, has a distinct counteracting effect on specific biological processes that are harmful to overall brain health and subsequent cognitive function (Feart et al., 2010). Particular biological risk factors that are suggested to be primary factors in the aetiology of age-related cognitive impairment, and pathological neurodegeneration include, oxidative stress, neuroinflammation, insulin resistance, and reduced cerebral blood flow (Kahn and Suzuki, 2010; Lovell and Markesbery, 2007; Scarmeas et al., 2006).

Individually, each of these biological factors are particularly injurious in the ageing brain due to their negative impact on neuronal and cell-signalling pathways, and subsequent dysfunctions in the neuroendocrine regulators of cognitive processes. Oxidative stress is commonly defined as an imbalance between the production of reactive oxygen species (ROS) and biological antioxidant defences (Betteridge, 2000). Increased production of ROS state in the brain is associated with apoptotic cell death of neurons and increased oxidatively damaged DNA, lipids and Apolipoprotein E4 (ApoE4), leading to accelerated cognitive ageing.
Neuroinflammation is a complex process in the brain that responds to all the cells within the central nervous system, including glial cells (i.e. microglia, macroglia and astrocytes), neurons and leukocytes. Chronic inflammation compromises the integrity of the blood brain barrier (BBB), allowing higher levels of irritants to enter the brain, and subsequently increasing the production of inflammatory cytokines, such as interleukin-1β (IL-1β) and tumour necrosis factor-alpha (TNF-α). Inside the brain these inflammatory cytokines impair adult neurogenesis (i.e. production of new neurons), which are vital for learning, memory and cognitive function (O’Callaghan et al., 2008).

Insulin is a peptide hormone produced by the pancreatic β-cells that is crucial for brain function due to its role in modulating glucose uptake, and protecting the health of brain cells (i.e. their functioning, growth and survival) (Convit, 2005). Generally, the plasma level of glucose in the brain is relatively stable, however even small changes in glucose levels can alter metabolic homeostasis, which has been consistently linked to insulin resistance (i.e. where the cells in the body become resistant to insulin upon glucose uptake, leading to hyperglycemia) and cognitive impairment in older individuals (Meier-Ruge et al., 1994).

Accumulated evidence from recent studies have shown that higher adherence to the MedDiet pattern is associated with reduced interleukin 6 levels and C-reactive protein (hsCRP) inflammatory markers (Gu et al., 2010); reduced markers of oxidative stress (Mancini et al., 1995); reduced insulin resistance and plasma glucose levels (Esposito et al., 2004), and improved endothelial function (Vogel et al., 2000). Thus, it is likely that these specific biological risk factors (i.e. inflammation, oxidative stress, metabolic abnormalities and reduced cerebral blood flow) are involved in the pathway between the whole MedDiet pattern and age-related cognitive outcomes, and should therefore be considered as potential mediators.

Presently, a clear understanding of how the MedDiet pattern effects such biological risk factors has not come to light. However, taking a look at some of the key components in the MedDiet individually may assist in arriving at a clear picture of how the whole diet exerts its neuroprotective properties. Perhaps, the exceptionally high amount of antioxidant-rich foods (e.g. dark green leafy vegetables, asparagus, tomatoes, onions, tree nuts, citrus fruits, red wine, pulses, whole grains) in the MedDiet may be one of the most valid explanations for benefit (see Appendix 1). Indeed, dietary antioxidants with important phytochemicals have been highlighted in the literature for their potential to exert a multitude of neuroprotective actions in the ageing brain, including the potential to prevent or reverse age-related losses in cognitive performance (Youdim and Joseph, 2001). This postulated neuroprotective potential appears to be underpinned by several key actions. Firstly, dietary antioxidants have been found capable of blocking oxidative-induced damage to existing neurons, neurogenesis production, and mitochondria by inhibiting the activation of caspase-3; a predominant caspase protein involved with amyloid-beta precursor protein (APP) during apoptosis (i.e. alterations in synaptic plasticity, neuronal death and subsequent hippocampal-dependent memory impairment) (Schroeter et al., 2001).

Secondly, antioxidants have been shown capable of inhibiting, preventing and/or repairing damage induced by neuroinflammation. This effect appears to be via mechanisms that include inhibiting free radicals (i.e. nitric oxide, NO) and cytokine production (i.e. IL-1β and TNF-α) in activated microglia cells, suggesting a potential to reduce apoptotic death of neurons. This is particularly important given the role of neuronal apoptosis in the pathogenesis of neurodegenerative diseases such as AD (Lau et al., 2007).

Third, flavonoids, one of the most abundant types of dietary antioxidants, have been shown to improve endothelial function and cerebral blood flow (Fisher et al., 2003). Using transcranial Doppler ultrasonic (TCD) techniques, Sorond et al. (2008) found that after the consumption of a flavanol-rich cocoa drink, peripheral vasodilation was induced in a NO-dependent manner, and significantly increased blood flow to the brain through the middle cerebral artery. Taken together, these findings suggests dietary antioxidants hold potential means for protecting the brain from oxidative and inflammatory-induced damage, and improving cerebral blood flow (CBF), which is important given the robust role these processes play in cognitive ageing and in the development of dementia (Scarmeas et al., 2006).

From a theoretical standpoint, it seems plausible that the abundant antioxidant concentrations in the MedDiet alone are likely to play a fundamental role in MedDiet - cognitive ageing association (Visioli and Galli, 2001). However, it is possible that other key biornutrients and foods of this diet also contribute to such postulated benefit. Indeed, converging evidence from recent supplement interventions and cross-sectional studies have demonstrated support for this notion. Other individual nutrients that have been shown to be particularly important for age-related cognitive function, and also found within the traditional Cretan MedDiet pattern, include: both plant-derived; α-Linolenic acid (ALA) (Willis et al., 2009) and marine-derived; long-chain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) n-3 polyunsaturated fatty acids (PUFAs) (Sinn et al., 2010); monounsaturated fatty acids (MUFA) (Naqvi et al., 2011); vitamins B6, B 2 and folate (Bryan et al., 2002) and minerals, including magnesium, iodine, selenium, potassium, zinc and iron (Simopoulos, 2001). In fact, the elevated levels of PUFAs and MUFA’s found in the MedDiet pattern, particularly from high fish, nut and olive oil consumption, is another element of this diet potentially contributing to postulated cognitive preservation in older age. For example, long-chain n-3 dietary PUFA’s have been found in recent research to be neuroprotective modulators via their impact on cholinergic functioning (Aid et al., 2003). The “cholinergic hypothesis” asserts that degeneration of cholinergic basal forebrain neurons, and the associated termination of neurotransmission in the hippocampus, cortex and amygdala, plays a distinctive role in cognitive deterioration that occurs during the ageing process, and in the development of AD (Terry and Buccafusco, 2003). Robust support for the cholinergic theory has been shown by evidence in a number of animal studies (Aid et al., 2003; Favreliere et al., 2003) which have shown that dietary supplementation of PUFAs increased acetylcholine (Ach) synthesis via inhibition of Ach hydrolysis, in turn, modulating cholinergic activity in the hippocampus and cortex of rats.

In humans, the aged brain has been shown to display subordinate levels of PUFA in neuronal membranes, and lower levels of phospholipid-bound fatty acids in the cortex and hippocampus when compared to the young brain. It is proposed that this reduced level of PUFA is a key factor contributing to observed declines in neuronal function in the older adult brain (Ulmann et al., 2001). Taken together, these findings indicate that consuming a diet with foods high in PUFAs may influence sustained optimal cholinergic functioning during the ageing process, which may subsequently promote greater age-related cognitive function.

Another contributing factor for benefit may relate to the high amounts of olive oil typically found in the MedDiet. Notably, olive oil contains particularly high levels of caffeic acid and tyrosol. The influence of these phenolic compounds in reducing markers of inflammation in the CNS (i.e. reduce interleukin-6 production in peripheral blood mononuclear cells and white blood cell counts) is well documented (Bulotta et al., 2014; Sanchez-Moreno et al., 2006). As such, there may be a potential of olive oil to promote age-related cognitive function via the ability to suppress neuroinflammation.

The evidence reviewed so far is based on the assumption that individual nutrients contained in the food components of the Med-
Diet may assist in delaying the onset of age-related cognitive impairment via their own, unique, neuroprotective mechanisms. However, this notion neglects a very important, unexplored relationship among the multiple foods and nutrients from the whole MedDiet, where the potential for an even greater multifactorial, synergistic effect may occur on a molecular level. For example, a noteworthy example of synergism among nutrients is found between the vitamins C and E and carotenoids. Vitamin E has been shown to work synergistically with vitamin C by reinstating its free radical scavenging activity (Sies, 1997), and carotenoids in association with vitamin E can amplify their effect against free radicals (Paiva and Russell, 1999). In addition, while antioxidant enzymes have been found capable of protecting neurons from oxidative-induced injury, this effect requires dietary minerals such as, copper, zinc, manganese and selenium as cofactors, along with amino acids for synthesis (Machlin and Bendich, 1987). Furthermore, laboratory animal studies investigating the feasibility of modifying AD pathology have shown the human endogenous, antioxidant defence system (e.g. catalase [CAT], superoxide dismutase [SOD], glutathione peroxidase [GPx]) is known to be deficient without the synergistic effects of exogenous antioxidants, such as vitamin E, vitamin C, polyphenols and carotenoids. For this reason, the traditional MedDiet pattern, abundant in foods which contain both endogenous and exogenous type antioxidants, may be expected to synergistically produce an antioxidant defence system that is particularly powerful in its effects on the ageing brain, supporting further protection against age-related cognitive dysfunction.

3. The contemporary Western diet

3.1. The association between the contemporary Western dietary pattern and age-related cognitive function

In the scientific literature (Kanoski and Davidson, 2011; Hu, 2002; Francis and Stevenson, 2013; Cordain et al., 2005) the Western diet is mainly characterised by high intakes of processed food, red meat, full-fat dairy, processed meats, alcohol, high energy, saturated fat and refined sugars and low intakes of vegetable and fruit, fibre, and complex carbohydrates, with a typical n-6 (arachidonic acid, ARA) to n-3 (DHA) fatty acid ratio found around ~10–20:1) (Molendi-Coste et al., 2011; Drewnowski and Popkin, 1997; Farooqui, 2009).

Throughout history, urbanisation, supermarketeisation and globalisation of food systems has seen the Western diet and lifestyle spread ubiquitously worldwide, including in developing countries (Schiff, 2005). Consequently, in line with the rising popularity of foods that are high in saturated fats and refined sugars, so too has the incidence of adverse health consequences and chronic diseases, including obesity, (Bray and Popkin, 1998), type 2 diabetes mellitus (Gross et al., 2004), and cardiovascular disease (Hu et al., 1997). Although there is great angst for the rising incidence of many health-related problems, the rise in obesity prevalence in some Western countries (i.e. 65% in the US, 81% in Australia, 93% in New Zealand and 66% in the UK) since 1980 (Ng et al., 2014) is of particular concern as it tends to be a major precursor to many other health-related issues such as metabolic syndrome, as well as chronic diseases including type 2 diabetes mellitus, hypertension, stroke, cardiovascular disease and certain forms of cancer (WHO, 2015).

The detrimental effect of obesity on cognitive outcomes, particularly increased risk of developing MCI, AD and dementia, is also now becoming more apparent. Indeed, a number of recent longitudinal studies have shown that obesity in mid-life is associated with a 70–100% increased risk of developing AD and dementia in older age (Kivipelto et al., 2005; Whitmer et al., 2005). Furthermore, it is now becoming evident that the clinical problems related to obesity are translating to effects on brain physiology and function. For example, a number of studies have confirmed a link between clinical obesity and alterations in brain morphology such as reductions in focal grey matter volume, hippocampal pathology and enlarged orbitalfrontal white matter (Panacciulli et al., 2006; Kanoski and Davidson, 2011). Other studies have collectively shown that obese patients perform significantly worse on memory, learning and executive function tasks when compared to non-obese individuals (Waldstein and Katzel, 2006; Elias et al., 2003). Therefore, it is possible that high consumption of diets rich in saturated fats, refined sugars and processed foods may in fact mediate the relationship between obesity and cognitive dysfunction.

Of the few studies which have investigated the association between the Western diet and age-related cognitive function among human populations, most have primarily focused on the two main elements of the Western diet; saturated fats and simple carbohydrates (mono and disaccharides, e.g. sucrose and glucose). Nevertheless, among the evidence drawn from this body of literature, there is a compelling consensus for the detrimental health consequences of high consumption of saturated fats and sugar on age-related cognitive function and neurodegenerative disease (See Table 2). In a prospective study investigating the effects of saturated fats on the development of AD, Morris et al. (2003) found among 815 community dwelling older adults aged 65 years and over, participants with the highest intake of saturated fat were 2.2 times higher risk of incident AD compared to those with the lowest intake (p = 0.39; 95% [CI], 1.1–4.7). Added evidence for the detrimental effects of high saturated fats on AD risk, and age-related cognitive function were demonstrated in Bayer-Carter et al. (2011) RCT, in which 49 older adults (20 cognitively healthy; 29 with MCI) her a HIGH diet (45% fat; 35–40% carbohydrates [glycemic index ≤70]; 15–20% protein) or a LOW diet (25% fat; 55–60% carbohydrates [glycemic index ≤5]; 15–20% protein for four weeks. Participants were tested at the end of the trial on a number of cognitive tests, as well as an oral glucose tolerance test and cerebrospinal fluid (CSF) sampling for the measurement of ApoE. Results indicated that CSF ApoE levels were increased by the LOW diet and decreased by the HIGH diet for both groups (i.e. healthy older adults and those with MCI). In addition, the LOW diet decreased insulin, plasma lipids, and CSF F2-isoprostane concentrations, while the HIGH diet conversely increased all of these mechanisms for both groups. Maintenance of the LOW diet for four weeks also improved delayed visual memory for both groups when compared to those who were on the HIGH diet. Even though the duration of this RCT was only four weeks, the findings are nonetheless valuable in they suggest a diet high in saturated fat and sugar may modulate the risk of AD and impair cognitive function through its effects on the CNS via lipoproteins, insulin and oxidative stress.

Morris et al. (2006) found participants with high dietary intake of saturated and trans fats, in conjunction with high intake of copper, were significantly associated with accelerated cognitive decline (α 143% increase in the decline rate) compared to those with low intake of saturated and trans fats together with copper. Alarming, among those participants in the top 20% for highest saturated fat with copper intake, the increase in decline rate was equivalent to 19 more years of cognitive ageing. Finally, investigating the impact of whole dietary patterns, Akbaraly et al. (2009) found among 4693 stroke-free male and female older European participants with high intake of a Western-type dietary pattern including, sweet desserts, processed meat, fried food, chocolates, refined cereals, margarine, quiche/pie, and high-fat dairy products on age-related cognitive function, had higher odds ratio of age-related cognitive impairment for reasoning (odds ratio (OR) = 1.55; 95% confidence interval (CI) = 1.21–1.98), vocabulary (OR = 2.36; 95% (CI) = 1.84–3.04), phonemic (OR = 1.70; 95% CI = 1.33–2.19) and
Table 2
Principal empirical studies investigating the association between high saturated fat and Western-type dietary patterns and age-related cognitive function.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study population</th>
<th>Study design follow-up</th>
<th>Sample size</th>
<th>Mean age (SD)</th>
<th>Cognitive outcomes</th>
<th>Efficacy</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albaraly et al. (2009)</td>
<td>Older adults</td>
<td>Cross-sectional</td>
<td>4,693</td>
<td>61.2 (6.2)</td>
<td>Age-related cognitive impairment</td>
<td>▼</td>
<td>Participants with higher intake of the ‘processed food’ dietary pattern had higher odds ratio of age-related cognitive impairment compared to those with a low intake</td>
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<td></td>
<td>London</td>
<td>(no follow-up)</td>
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<tr>
<td>Bayer-Carter et al. (2011)</td>
<td>Older adults USA</td>
<td>Randomized controlled trial (4 weeks)</td>
<td>49</td>
<td>68.5 (not given)</td>
<td>Age-related cognitive performance, AD risk</td>
<td>▼</td>
<td>Participants randomized to the HIGH diet (i.e. 45% saturated fats, 35%–40% carbohydrates (glycemic index, &gt;70), and 15%–20% protein) for 4 weeks were found to have moved cerebrospinal fluid (CSF) AD biomarkers in a direction that may influence the presymptomatic stage of AD (i.e. before plaque deposition). However, reduced cognitive performance was not observed among those randomised to the HIGH diet group, suggesting there was either no effect or perhaps 4 weeks of exposure was not long enough to manifest negative effects in cognition</td>
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<td>Eskelinen et al. (2008)</td>
<td>Older adults</td>
<td>Longitudinal (21 years)</td>
<td>1,449</td>
<td>71.1 (4.0)</td>
<td>Age-related cognitive performance, MCI risk</td>
<td>▼</td>
<td>After all adjustments abundant saturated fat (SFA) intake at midlife was associated with poorer prospective memory and global cognitive function in older age, and also with an increased risk of MCI (OR = 2.36; 95% (CI), 1.17–4.74)</td>
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<td>Kalmijn et al. (2004)</td>
<td>Middle &amp; older adults</td>
<td>Cross-sectional (no follow-up)</td>
<td>1,613</td>
<td>56.3 (7.1)</td>
<td>Age-related cognitive impairment risk</td>
<td>▼</td>
<td>Higher dietary cholesterol intake was found significantly associated with an increased risk of impaired cognitive flexibility (OR = 1.26; 95% (CI), 1.01–1.57 per SD increase) and also memory (OR = 1.27; 95% (CI), 1.02–1.57)</td>
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<td>Netherlands</td>
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<tr>
<td>Morris et al. (2003)</td>
<td>Older adults</td>
<td>Longitudinal (3.9 years)</td>
<td>815</td>
<td>73.1 (not given)</td>
<td>Risk of incident AD</td>
<td>▼</td>
<td>In a multivariable model adjusted for sex, education, race, and ApoE4, participants with the highest intake of saturated fat were found to have 2.2 times higher risk of incident AD compared to those with the lowest intake</td>
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<td>USA</td>
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<td>Morris et al. (2004)</td>
<td>Older adults USA</td>
<td>Longitudinal (6 years)</td>
<td>2560</td>
<td>≥65.0</td>
<td>Age-related cognitive decline</td>
<td>▼</td>
<td>In separate mixed models participants with higher intake of saturated fat (p-trend = 0.04) and trans-unsaturated fat (p-trend = 0.07) were associated with greater linear decline in cognitive function over 6 years</td>
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<tr>
<td>Morris et al. (2006)</td>
<td>Older adults USA</td>
<td>Longitudinal (6 years)</td>
<td>3,718</td>
<td>74.3 (not given)</td>
<td>Age-related cognitive decline</td>
<td>▼</td>
<td>Participants with high dietary intake of saturated and trans fats, in conjunction with high intake of copper, were found significantly associated with accelerated cognitive decline (a 143% increase in the decline rate) compared to those with low intake of saturated and trans fats together with copper</td>
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<tr>
<td>Okereke et al. (2012)</td>
<td>Older adults USA</td>
<td>Longitudinal (4 years)</td>
<td>6,183</td>
<td>71.9 (not given)</td>
<td>Trajectories of cognitive change</td>
<td>▼</td>
<td>Older aged participants with higher saturated fat intake were significantly associated with poorer ageing trajectories for global cognition (p for linear trend ≥ 0.008) and also verbal memory (p for linear trend ≥ 0.01)</td>
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</table>

Abbreviations: AD = Alzheimer’s disease; CI = confidence interval; MCI = mild cognitive impairment; p value = statistical significance less than 0.05; OR = odds ratio
Efficacy values: ▼ = Western-type diet improved outcomes, -Western-type diet had no effect, ▼ = Western-type diet had a detrimental effect on outcomes.
semantic fluency (OR = 1.58; 95% CI = 1.25–2.01) compared to participants with high intake of a ‘whole food’ dietary pattern (i.e. leafy vegetables, other vegetables, tomatoes, fruits, fish, salad dressing, peas and dried legume). Of note, this association was seen after adjusting for age, sex, education and energy intake.

The data discussed above from human studies is indeed limited, however is well supported by experimentally controlled animal research. A compelling body of studies have put forth evidence for a cause-effect relationship between the Western diet and cognitive function among lab animals through means of directly manipulating the diet. For example, on cognitive tasks such as the Radial Arm Maze and Morris Water Maze, spatial memory performance has consistently been shown to be impaired in mice and rats randomised to maintain diets specifically high in sucrose (Cao et al., 2007), saturated fat (Greenwood and Winocur, 1996), and in diets high in both refined sugar and saturated fat (Stranahan et al., 2008) when compared to rats allocated to control diets (standard rat Chow; low% of fats). A further number of well-controlled animal studies have shown evidence that diet-induced obese rats fed a Western diet (i.e. high in energy, saturated fat and dextrose; 38% kcal from carbohydrate, 21% kcal from protein, and 40% kcal from fat) exhibited significantly worse cognitive performance on set tasks compared to control diet resistant rats and rats fed a CHOW diet (Davidson et al., 2013; Kanoski et al., 2010), suggesting that high consumption of Western diet may mediate the relationship between obesity-induced cognitive impairment.

Taken together, it is plausible that a similar causal link may also exist between Western dietary intake and impaired age-related cognitive function in older human adults. However, while animal models provide the closest approximation to a human response, they are of course never exact. Differences in anatomical and physiological factors may occur. Thus, it may be difficult to extrapolate with precision what animal data suggests for human beings. Further human RCTs with larger sample sizes and of longer duration will be needed to strengthen validation of this assumption.

3.2. Underlying mechanisms of the Western dietary pattern on age-related cognition

As with the MedDiet, a clear understanding of the underlying mechanisms relating to the association between Western dietary intake on age-related cognitive function has not been established. Perhaps the most convincing theory to date relates to the effects of Western dietary consumption on two brain regions fundamentally involved in age-related cognitive function; the prefrontal cortex (PFC) and the hippocampus (Francis and Stevenson, 2013). The PFC is well established in playing a key role in the development and maintenance of a collation of cognitive abilities that form the executive functions and that are sensitive to age-related decline. These abilities include verbal fluency, focussed and sustained attention, inhibition and working memory (Anstien and Li, 2005; Curtis and D’Esposito, 2003). Likewise, the hippocampus is well known for its support in the acquisition of forming new memories (Scoville and Milner, 2000), and is also particularly important in the maintenance of spatial and episodic memory (Cohen and Eichenbaum, 2001).

While all areas of the human brain are greatly sensitive to the effects of ageing and also diet, the PFC and the hippocampus appear to be particularly vulnerable to both. Among diet-related variables, the high saturated fats and sugars found typically in the Western diet have been identified as the greatest risk factors to these two brain regions during the ageing process (Francis and Stevenson, 2013). Specifically, it is postulated that excessive consumption of saturated fats and sugars may set in motion several potentially injurious neurophysiological changes in the PCF and hippocampus, including molecular abnormalities in mitochondrial function and trophic factors (e.g. nerve growth factor, NGF), promoting both the facilitation of protein aggregates (e.g. Aβ, Lewy bodies, neurofibrillary tangles), and also higher levels of toxic biological mechanisms accumulating the brain, including oxidative oxidative stress, neuroinflammation, insulin resistance, and dietary-induced reductions in brain derived neurotrophic factor (BDNF) (Farooqui, 2014). Overtime these types of detrimental changes in the brain may subsequently lead to impairment in age-related cognitive functioning (Francis and Stevenson, 2013) (See Fig. 1).

Indeed, it has become apparent that changes in cholesterol balance caused from excessive saturated fat intake may produce modifications in the expression of apoliprotein E (ApoE) and sterol recycling in the brain, subsequently damaging neurons and glial cells (Dietschy and Turley, 2001). It is well documented that among patients with AD thesterol flux across the central nervous system (CNS) is elevated (Lütjohann et al., 2000), and in mouse models, mice given a high-fat diet increases levels of cholesterol and amyloid plaque load in the brain (Refolo et al., 2001).

Furthermore, while glucose is the primary source of fuel for the brain, over abundance of refined sugars (stored in the form of glucose) can have a number of adverse effects, including blood vessel damage and hyperglycemia. Such damage to blood vessels in the brain, and hyperglycemia have been suggested to play a role in the pathogenesis of neurodegeneration leading to cognitive dysfunction (Kodl and Sequist, 2008). Indeed, higher glycated haemoglobin (HbA1C) levels in the brain are associated with a greater level of brain shrinkage (Kodl and Sequist, 2008; Starr and Convit, 2007). Even among non-diabetic populations, higher sugar consumption is associated with lower scores on a number of cognitive tests (Ye et al., 2011). In fact, the damaging effects of excessive glucose on the brain are so pronounced that even a single acute episode of hyperglycemia has been shown to reduce cognitive function in aspects of memory, global cognition, visual-spatial ability and visual-motor skills (Widom and Simonson, 1990).

How high levels of saturated fats and refined sugars exert such powerfully deleterious effects on the ageing brain remains ambiguous. However, a growing body of recent animal studies have proposed the association between Western dietary intake and age-related cognitive dysfunction is most likely mediated by certain biological risk factors, including inflammation, oxidative stress, insulin resistance and BDNF. For example, Beilharz et al. (2014) conducted an experiment to investigate the effects of a diet containing lard, cakes, biscuits, and a 10% sucrose solution (59% carbohydrate, 26% protein, 15% fat) on hippocampal-dependent memory performance among rats, and also examined the mediating role of inflammation on this inferred relationship. The results of this study indicated that rats fed components of a Western diet showed significant impairments in the recognition memory task in comparison to the control group (i.e. chow fed rats; 50% carbohydrate, 5% protein, 45% fat). Furthermore, rats exposed to a Western-type diet in this study exhibited increases in markers of hippocampal inflammation (i.e. TNF-α and IL-1β mRNAs), oxidative stress, plasma insulin, leptin and triglyceride, indicating potential mediating responses.

In relation to oxidative stress, various laboratory animals maintaining intake of a Western dietary pattern have been shown to develop significantly higher levels of oxidative stress and lipid peroxidation in the brain when compared to animals on control diets (Zhang et al., 2009). Studzinski et al. (2009) demonstrated that aged mice fed a high-fat Western diet (WD) chow for one month was sufficient to facilitate increases in lipid peroxidation levels and cerebral oxidative stress in mice, with preceding alterations in amyloid beta (Aβ). Given Aβ is the main element found within amyloid plaques, a key histopathological hallmark of AD (Kar et al., 2004), this finding is particularly important.

Insulin resistance is another risk factor assumed to play a key role in the relationship between the Western diet and age-related cognitive dysfunction, particularly in relation
to hippocampal-dependent memory (Greenwood and Winocur, 2005). A longitudinal study (Mielke et al., 2006) examining the effects of a Western-style diet on associative learning, found mice who were fed a Western-style diet for one year showed impaired performance in learning an operant bar-pressing task in comparison to those mice fed a control diet. Furthermore, results of this study revealed that mice on Western diet maintenance for one year exhibited increased insulin resistance and weight gain, impairment in glucoregulation, and reduced insulin-mediated signalling in the hippocampus. These findings suggest cognitive processing involved with associative learning and consolidation were negatively influenced by the effects of the Western diet, and that poor glycemic control and insulin resistance may have been intervening variables in this response.

Neuroplasticity within the brain involves the important ability of neurons to adapt to injury or disease, and adjust molecular and cellular mechanisms of neurite growth and synaptic structure and function in response to behavioural adaptation (Pascual-Leone et al., 2011) is a crucial signalling molecule within the brain that works intimately in the process of maintaining stability and survival of neuroplasticity, as well as other neuronal mechanisms (e.g. neurogenesis) that underlie cognitive abilities such as memory and learning (Calabrese et al., 2014). Evidence from a number of recent studies has indicated that rats fed a high caloric diet can impair neuroplasticity and subsequent cognitive functioning via decreased BDNF expression within the hippocampus and medial PFC, when compared to rats fed a low-caloric control diet (Kanoski et al., 2007; Molteni et al., 2002). Collectively, these findings show support for the detriment of consuming high amounts of saturated fats and refined sugars on age-related cognitive function, and highlight the mediating potential of oxidative stress, neuroinflammation, insulin resistance and reduced BDNF in this response.

While no clear mechanistic explanation involving these biological risk factors has been put forth in the literature, it has been proposed that consuming high levels of foods rich in ARA, with a limited amount of DHA and EPA containing foods may be one potential factor underlying such adverse, neurophysiological mediated changes to the PFC, hippocampus and all other areas of the ageing brain in general (Farooqui, 2009). ARA-derived lipid mediators, typically named eicosanoids, include leukotrienes (LTs), thromboxanes (TXs) and proinflammatory prostaglandins (PGs). Nonenzymic peroxidation of ARA is metabolised to 4-hydroxyxynonenedals (4-HNE), isoketals (IsoKs), isofurans (IsOFs) and isoprostanes (IsoPs). This group of ARA lipid mediators have been shown to play a role in the development of inflammation, oxidative stress, vasodilation, apoptosis and other harmful biological responses in the brain. In
both animals and humans, a diet enriched in ARA type foods has been shown to generate higher levels of pro-inflammatory LTs, TXs and PGs, which, in turn, increase the risk of neurodegenerative and cognitive impairment through increasing toxic biological processes developing in the brain and subsequently reducing less inflammatory cellular substrates (Faroqui, 2014).

In contrast, enzymic DHA-derived lipid mediators, namely docosanoids, are metabolized by 15-LOX-like enzymes and converted into D-series resorvins and neuroprotecorps (NTPs). Enzymic EPA-derived lipid mediators include E-series resorvins, 5-series LTs and 3-series PGs. Nonenzymic lipid mediators of DHA and EPA include 4-hydroxyhexenal (4-HHE) and neuroprostanes (NPs) for DHA, and cyclopentenone-isoprostanes (A3(1,1)-Isops). These metabolites work hard to counteract the effects of eicosanoids as well as modulating leukocyte trafficking and the expression of cytokines (Marcheselli et al., 2003). An accumulated body of studies have shown that ARA- and DHA-derived lipid mediators consistently compete with each other for the same enzymes. When the presence of n-6 linoleic acid (LA) in the brain is abundant over n-3 ALA the regulation and magnitude of inflammation, oxidative stress and overall homeostasis is compromised (Faroqui, 2009).

Importantly, ARA, DHA and EPA lipid mediators in neural tissues are somewhat regulated by diet. Diets containing high levels of n-6 ARA, such as the Western diet, increase levels of triacylglycerols (TGs), which, in turn, can reduce the amount of leptin reaching critical areas of the brain such as the PFC and the hippocampus. Subsequently, cognitive function may be impaired. In contrast, diets containing high levels of n-3 DHA and EPA, such as the MedDiet, protect brain development and functioning through regulating neural membrane fluidity permeability, enhancing receptor function and suppressing insulin resistance and neuroinflammation (Faroqui, 2009). Furthermore, in recent animal research diets enriched with DHA have been found capable of stimulating glucose and cellular metabolism, reducing oxidative stress, and also enhancing synaptic plasticity through the ability of modulating specific genes (i.e. mitochondria) which facilitate neurogenesis; the formation of new neurons, glial cells and astrocytes in the brain (Faroqui, 2009).

Additionally, there is evidence implicating the role of Western dietary intake in the generation of advanced glycation end products (AGEs) in the ageing brain. These highly toxic compounds are harmful to nearly every type of molecule and cell within the human brain, and are believed to play a key role in the development of oxidative stress, inflammation, insulin resistance, and many chronic age-related diseases, including AD (Vistoli et al., 2013). The main way human beings are exposed to exogenous AGES is through the ingestion of processed foods cooked at extremely high temperatures (e.g. deep-fried pastries, burgers, chicken and fries). Thus, another postulated pathway between the Western diet and age-related cognitive dysfunction may potentially occur via the mediated interactions of AGES.

A diagrammatic synopsis of the above sections on potential mechanisms linking the MedDiet and Western diet to age-related brain health and cognitive function is presented in Fig. 1.

4. The feasibility of Mediterranean dietary interventions in industrialised Western cultures

The most obvious determinant necessary to decipher whether a dietary intervention worked or did not, is evidence. Most commonly, this is conveyed in the literature by means of expressing the results, validity and reliability, and what study limitations may hinder interpretation of the study findings. Often one element that is not often considered or discussed in study findings, is the feasibility of a dietary intervention (i.e. the practicality of an intervention). As researchers, we are required to present findings from empirical research in a way that allows others (i.e. clinicians, practitioners, health care professionals, external Government bodies, policy developers, fellow researchers) to adequately answer the following questions when deciding upon the validity and feasibility of a study’s result: 1. “are the study results valid?”, 2. “can they be generalised to the wider population of interest?”, 3. “is the intervention a feasible approach, taking into account socio-cultural and economic factors together with available resources?”, 4. “what is the likelihood of the intervention producing a clinically meaningful effect?”. All of these questions need to be adequately addressed by studies before study findings and conclusions can be extrapolated to different populations and enforced in medical practices.

As presented above, a growing number of studies have shown evidence to suggest that adhering to a traditional MedDiet intervention that mimics dietary practices of populations in Crete Greece in the 1960–70s may benefit age-related cognitive function not only in Mediterranean populations, but in non-Mediterranean populations as well. However, the question of whether a MedDiet intervention could be feasible among Western cultures in a way that promotes lifestyle and dietary reform, is currently unknown. This is a timely question to consider at present, as more and more studies in non-Mediterranean countries are choosing to spend money, time and effort on investigating the benefits of the MedDiet on health outcomes. Having an understanding of whether a traditional MedDiet intervention can be maintained by individuals in the Western world once the study has completed would be highly valuable. This question will be addressed below in a way that helps elucidate potential reasons why the feasibility of a MedDiet intervention may or may not work in Western cultures. Two critical areas are discussed; 1. socio-cultural values, attitudes, and norms; and 2. palatability, availability, convenience and cost. Primarily, the discussion in this section relates to certain Western countries, including North America, Australia, New Zealand and the UK. Evidence for other diverse countries that consume a Western dietary pattern may vary.

4.1. Socio-cultural components of the Western diet versus the Mediterranean diet

In taking a closer look at the groundwork behind the establishment of the Western diet, throughout history, several revolutionary movements, including economic development, industrialisation, urbanisation, technological advancement, food market globalisation, materialism, individualism, consumerism, modernisation and a rapid increase in the affordability and availability of processed foods, refined grains and sugars, have each contributed in ways that have shaped the Western diet into what it has been described as by some today (Popkin et al., 2012).

Overtime, the appeal and adherence to the Western diet with sometimes cheaper, unhealthy convenience foods (e.g. fast foods, discretionary foods etc.) as part of its repertoire, has become a defining socio-cultural characteristic among modern Western populations (Cordain et al., 2005). In present times there have been numerous attempts by Government-funded marketing campaigns set up in the media, schools, medical clinics, and other social outlets to lower fat and sugar consumption and to eat more healthily, however the attitudes and eating habits of many Western individuals has not changed much over the years (Smith et al., 2013). For example, in the 2011–12 Australian Health Survey among 12,000 people, it was found that 30% less fruit and vegetables were being consumed compared to 15 years ago, and only 5.6% of Australian adults were eating the recommended daily intake of vegetables (AIHW, 2012; ABS, 2014). Similar findings have been documented for the UK (DEFFRA, 2014), the US (Moore and Thompson, 2015)
New Zealand (Roy Morgan and Research, 2014). In contrast, a much larger proportion of adults in some Western countries have been found to consume sub-optimal daily energy from discretionary foods (Poti et al., 2015; ABS, 2014). For example, in a large study conducted in the US (Poti et al., 2015) investigating house hold food purchases, over a two year period, it was found that 61% (more than three-fourths) of the food and beverages purchased were highly processed foods. In Canberra, Australia, a state-wide LiveLighter ACT survey (2015) revealed close to 30,000 people reported they consume around 23 kg or more of sugar over the year in the form of soft drink. Furthermore, among a number of industrialised Western countries, consumption of animal fats continues to rise (Amuna and Zotor, 2008). While these findings appear rather alarming, we must keep in mind that it is common for health food surveys to be based upon a 24-hour dietary recall. Thus, data generated from such surveys may only be capturing what people were eating on that particular day and may not necessarily be a true representation of the population’s overall eating habits.

Reasons why some people in Western countries may still be choosing to consume greater amounts of unhealthier food options over more healthier alternatives, despite public awareness, is somewhat unclear. The currently strained work-life balance operating as the socio-cultural norm in many Western countries is one proposed reason (Gatrell and Cooper, 2008). For example, in the US and Australia, recent population surveys revealed a significant percentage of adult men and women felt overwhelming stress and pressure to juggle work, family and personal commitments (APA, 2011, 2014; AFS, 2014). Increasing finances, taxes, job insecurity and other financial burdens (e.g. increased age to receive retirement benefits) appear to be primary reasons why Western mid-life and older adults are working extended hours, more than one job, and postponing retirement (McNamara and Williamson, 2013). Consequently, in the fight to keep up with such demands, lifestyle priorities such as eating healthy home cooked meals on a regular basis may simply not be achievable for some Western people, particularly for older adults who may be physically and financially limited, retired, or men who are unmarried or widowed (Edelstein, 2015).

In contrast to the socio-cultural underpinnings of the Western diet, the historical foundations for the traditional MedDiet have emerged through a lifetime of long-standing traditions, rituals, values and symbols that embrace hospitality, intercultural dialogue, large family and community sharing and gatherings, harvesting, fishing, animal husbandry and crop conservation (UNESCO, 2013). Consuming freshly cooked meals filled with an abundance of healthy foods and condiments (e.g. fruit and vegetables, whole meal grains, moderate red wine, olive oil, fish, nuts and seeds) as part of a regular diet, is documented as a cultural identity among Mediterranean populations (Willett et al., 1995). Fundamental lifestyle factors for traditional Mediterranean populations include: sharing lengthy meals with family and friends at home for relaxation and daily stress relief; enjoying tasty meals that have been carefully prepared and cooked during the day, to encourage eating healthy foods; and post-lunch siestas (afternoon naps), to provide an opportunity for daily relaxation and optimal sleep (Willett et al., 1995). Culturally, the act of drinking alcohol in traditional Mediterranean countries is well accepted, and more a general part of the everyday diet (e.g. a wine with lunch). Drinking alcohol to the point of intoxication, or to get “drunk”, as found in many Western cultures, is an uncommon practice in Mediterranean cultures (Martinez and Martin, 1987).

While many of these Mediterranean socio-cultural food and drinking traditions have warranted such high regard in the media and the scientific literature, over the past 30 or so years the eating habits of young, middle-aged, and even elderly individuals in Mediterranean countries have slowly evolved to a more “Westernised” pattern (Balanza et al., 2007; Tyrovolas and Polychronopoulos, 2011). The consequences of such adaptation has started to become very apparent. One example of this has been seen in the comparison of obesity rates between former and current Mediterranean older adult populations. In Keys et al. (1968) Seven Countries Study, a strikingly low number of obese older individuals living in populations of the Mediterranean region in the 1960s–70s, particularly in Crete, Greece (2–5%) were found. Recent analysis of obesity rates throughout Greece have shown a dramatic increase, with figures now showing an alarming number (<50%) of present older adults aged 65 years and above considered obese with body mass indexes (BMIs) greater than 30 (Ferro-Luzzi et al., 2002).

Although there is no sound evidence at present to suggest that adoption of certain Western dietary habits are solely responsible for the dramatic rise in obesity among current Mediterranean populations, from a sheer logical perspective, it seems highly likely. The fact that a number of past epidemiological studies have found the traditional MedDiet was inversely related to obesity (Keys et al., 1968; Schröder et al., 2004) provides some level of support for this notion. For age-related cognitive outcomes these findings are rather important, for as mentioned above, the link between obesity and cognitive impairment is well established. Thus, further investigation should be dedicated to explore whether the Western diet is indeed empowering an obesogenic environment among older adults in non-Western countries around the world.

4.2. The influence of food palatability, availability, convenience and cost

The phenomena of shifting traditional dietary behaviours concurrently with economic, demographic and epidemiological changes is known as the “nutrition transition” (Drewnowski and Popkin, 1997). This term has been used to describe the transition of non-Western populations from traditional diets to a Western-type diet, such as in the findings of Balanza et al. (2007) mentioned above. Having an understanding of the certain barriers that prevent people from improving and/or changing their diet is important. Among many factors that have been documented in the literature, it appears that key barriers for people in industrialised Western countries are palatability (Folkenberg and Martens, 2003), availability (Morland et al., 2002), convenience (Anderson et al., 2011) and cost (Darman and Drewnowski, 2008). Indeed, in a large health survey in the UK in 2007 (Thompson, 2007), qualitative data revealed that the top three reasons preventing people from changing their diet were 1. “it is too hard to change my eating habits”, 2. “I do not have time”, and 3. “it costs too much”.

When it comes to the palatability of foods, studies have found the most palatable and enjoyable foods are unquestionably those high in fat and energy-dense (Drewnowski, 1997). For many individuals, when faced with the choice of choosing between certain foods, energy-dense foods are found to be of preference over low-energy vegetables, fruit, grains, pulses and legumes (Drewnowski, 1998). High-fat foods and high-sugar foods, appear to have a sensory appeal that is difficult to resist for many human beings (Folkenberg and Martens, 2003). In fact, sugar has been suggested to have “drug-like” effects in the reward system of the brain due to its strong palatable, reinforcing effects (Ahmed et al., 2013). This powerful effect has been demonstrated by Lenoir et al. (2007) study where rats were given the choice of pressing one of two levers for either access to sugar-sweetened water or a dose of intravenous cocaine. Alarming, the results showed a significant number of rats (94%) chose the sugar over the cocaine ($F(28,1106)=8.71, p<0.01$), demonstrating the potently addictive effects of sugar.

A number of mechanistic explanations have been proposed for this phenomena. Most notably, orosensory properties of “taste” seem to be linked to a combination of texture, olfaction and taste
PATHWAY LEADING TO COGNITIVE IMPAIRMENT

Psychological risk factors
- Anxiety, Stress, Depression, Sleep Dysfunction, Loss of self-control

Non-modifiable risk factors
- Ageing
- Past Education
- Genetics

Western socio-cultural
- Large growth in: economic development, prosperity, industrialisation, urbanisation, technological advancement, agriculture and animal husbandry, food market globalisation, commercialisation, materialism, individualism, consumerism, and modernisation
- Increase in the affordability and availability of processed foods, sugary products, refined grains, lack of sleep and exercise

Western diet
- High intake of saturated and trans fats
- High energy
- High red meat
- Processed meats
- High alcohol (e.g., beer, spirits)
- Reduced fibre, vegetables, fruit
- Complex carbohydrates
- Processed foods (e.g., McDonald’s fast food)

Biological risk factors
- Mitochondria dysfunction
- Impaired oxidative stress
- ROS
- Sympathetic plasticity, neurogenesis, neurotransmitter synthesis, neuroendocrine (IGF2) and, neurosteroids (BDNF) function and transmission
- Lipid peroxidation
- Reduced risk of necrosis (cell death)
- and apoptosis (neuronal death)
- Enhanced IGF and BDNF function and transmission, synaptic plasticity, neurogenesis, neurotransmitter synthesis
- Cardiovascular disease
- Metabolic syndrome

Age-related Cognitive Function

Mitochondria homeostasis
- Reduced free radicals (i.e., ROS
- Optimal ATP energy production and redox regulation from ROS
- Reduced risk of oxidative stress
- DNA damage and lipid peroxidation
- Reduced risk of necrosis (cell death)
- and apoptosis (neuronal death)
- Enhanced IGF and BDNF function and transmission, synaptic plasticity, neurogenesis, neurotransmitter synthesis
- Greater cardiovascular health

Mediterranean diet
- Extra virgin olive oil
- High intake of fish (e.g., salmon, mackerel, herring)
- High intake of vegetables, particularly green leafy
- Legumes, seeds and nuts
- Leafy greens, sunflower seeds
- Wholegrain cereals/bread
- Moderate red wine intake
- Dried herbs (e.g., basil, thyme, oregano)
- Very low intake of processed food, red meat, cows

Mediterranean socio-cultural
- Rituals, symbols and long-standing traditions involving: harvesting, fishing, animal husbandry, crops conservation, cooking, processing large family and community sharing
- Eating together as a cultural identity and social exchange among Mediterranean communities
- Emphasis on values of hospitality, intercultural dialogue, creativity, neighbourliness, respect for diversity
- Transmit such values to new generations
- Markets filled with fresh produce

Protective Dietary factors
- Antioxidants: vitamins E, C, A, B, D, polyphenols, flavonoids, CoQ10
- Minerals: iron, zinc, iodine, magnesium, potassium, calcium, iodine
- Monounsaturated fatty acids (MUFA’s)
- Polyunsaturated fatty acids (Omega-3 PUFA’s)

PATHWAY LEADING TO COGNITIVE PRESERVATION

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Fig. 2. A model of potential biopsychosocial factors and inter-related pathways linking the MedDiet to preservation and the Western diet to impairment in age-related cognitive function.

(Schiffman et al., 1998). The decadent element of palatability (i.e., pleasantness) of food is an integral factor for the sensory profile of any given food. More specifically, the sensory perception of food involves the detection of odors, tastes, and certain textural attributes of the food. This initial stage is called “chemosensation”, and is followed by sending an integrated set of signals to the brain. Upon this sensory input, activated receptors in the nasal and oral cavities act on secondary messengers, from which we then become consciously aware of certain tastes, aromas and textures of food (Kringelbach and Berridge, 2010).

Another consideration when discussing the feasibility of the MedDiet in Western cultures is the availability, convenience and cost of foods. Indeed, food choice has been shown to be directly influenced by the availability and variety of foods in local supermarkets, along with the ease of access to the supermarket (Morland et al., 2002). Presently, the media have brought attention to the MedDiet in Western countries, publicizing many ways that people can incorporate it into their daily lives. However, truly adopting a MedDiet, particularly one that stems from traditional origins, may not be as easy as it has been portrayed in many Western-based cookbooks, news articles, and other marketing outlets. In countries such as Australia, America, UK and New Zealand, certain geographical, environmental and socio-cultural factors (e.g. urbanisation, industrialisation, economic development, and the affordability and availability of certain foods) may not enable individuals to adhere to a MedDiet in the same way that would typically be followed in Mediterranean countries.

Some examples of traditional Mediterranean foods found in the diets of those populations in the 1960–70s that are more or less absent from the shelves in a typical Western supermarket are: Kolokythoanthoi (zucchini flower), fried wet salted cod, mizithra cheese, paximadi (Greek rusk bread made from barley and softened with wine before eating), blessed thyme, snails, chilipotes pasta, fish roe salad, and Cretan dittany or “diktamos” (a wild herb only found on the island of Crete) (Trichopoulou et al., 2006). Thus, it may prove quite difficult for some people in Western cultures to locate and purchase specific Mediterranean foods and condiments on a regular basis. Moreover, it may be rather expensive to have certain foods imported such as the diktamos herb.

The appeal of food convenience has been reported as another major contributor of food choice in Western countries (Anderson et al., 2011). With large fast food chains on nearly every corner street in many Western countries, the ease of simply driving through an establishment to order a meal and have it cooked in a very short period of time at a reasonable price, is very appealing to many people who work long hours, do not have the time or the physical ability to cook, or who struggle financially (Anderson et al., 2011).

An additional determinant of the amount and type of food consumed is cost (Darmon and Drewnowski, 2008). An accumulated body of research has shown evidence that diet quality, morbidity and mortality rates in industrialised Western countries follows a socioeconomic gradient (Pappas et al., 1993; Kunst et al., 1998). In particular, the consumption of fresh fruit and vegetables, lean meat, fish, whole grains, and low-fat dairy products are suggested to be more likely consumed by those individuals with a higher socio-economic status (SES). Whereas, consumption of high-energy foods, refined grains, and saturated fats are associated with lower SES (Diez-Roux et al., 1999). As such, innate preferences for particular choices in diet seem to be related to the cost of food and one’s income. Indeed, recent statistics taken from the EMMA (2014) report revealed that two thirds of the Australian population sampled chose price and convenience as the most popular reasons for eating out at fast food chains rather than having a cooked meal at home. Similar findings have been documented for US populations (Smith et al., 2013).

As healthier foods (e.g. kale, spinach, salmon, chicken, tomatoes, fruit) tend to cost more than energy-dense foods (e.g. tinned fruit, commercial cereal, baked beans, fast food) (Rao et al., 2013) it becomes more understandable why some Western older individuals maybe choosing a less expensive, more palatable Western-type diet over a more costly, harder to access plant-based MedDiet.
Particularly, since a number of older Western adults may likely be retired, less mobile and supported by a Government pension, affording a nutrient-dense MedDiet regularly may simply not be achievable for some people.

In an attempt to accommodate for the factors aforementioned (i.e. palatability, availability, convenience and cost), a potential strategy may be to develop a “Westernised” MedDiet intervention, that is matched with the traditional MedDiet in terms of nutrient content, however uses more commonly available foods in Western countries. Indeed, in a recent pilot study conducted in Australia (Davis et al., 2015), among \( n = 10 \) older Australian adults, it was found that 87% of the study sample met a high level of compliance to an Australianised MedDiet, which was based closely around the exact nutrient content of the traditional MedDiet, however included a mixture of Mediterranean and non-Mediterranean foods that are easily available in Australia (e.g. wholesome breakfast cereal, reduced fat flavoured Greek yoghurt, tuna, avocados, canned pulse mix). As such, this type of an intervention may afford older Western older adults similar hypothesised nutrient benefits, however, provide a greater likelihood of achieving feasibility.

In an attempt to draw together the above sections discussing both the MedDiet and the Western diet, a novel biopsychosocial model has been developed to illustrate in a diagrammatic way, how biological, psychological and socio-cultural factors of both the MedDiet and Western dietary pattern may intervene either directly or indirectly through various pathways to promote either impairment or preservation of age-related cognitive functioning (See Fig. 2). In this model it is proposed that there are fixed factors, which are not amenable to change (e.g. gender, age, past education, genetics), and also tractable factors, which are more variable and adaptive (e.g. dietary and lifestyle behaviour, level of physical and social activity, psychological and biological risk factors). Psychological risk factors (e.g. anxiety, stress, depression, sleep dysfunction and loss of self-control) have not been discussed in detail in the present review, however their influence on age-related cognitive function can be viewed in a broader way in the biopsychosocial model.

5. Conclusions

To our knowledge, the present review was the first of its kind to examine the literature on comparing the MedDiet and the Western diet on age-related cognitive function, focusing specifically on the relevance for Western older adult populations. The primary aim of this review was to address two main questions that foresee whether or not the MedDiet is a feasible approach to preserving cognitive function and reducing risk of dementia for older adults, specifically in Western countries.

In synthesis with the reviewed literature, the evidence highlights the MedDiet as a potential therapeutic dietary pattern with a unique cocktail of multiple bioprotective nutrients, along-side a more balanced ratio of n-6:n-3 fatty acids from vegetable, marine and animal sources. Synergistically, at a molecular level, the interaction between these components may exert a multifactorial neuroprotective effect that is capable of enhancing age-related cognitive function through attenuating biological risk factors (i.e. inflammation, oxidative stress, metabolic abnormalities and suboptimal cerebral blood flow), and amplifying mitochondrial homeostasis, BDNF function and neuronal and cell-signalling pathways in the ageing brain.

In contrast, excessive consumption of a Western-type dietary pattern has been insinuated as a potential factor leading to pathology cognitive ageing and age-related cognitive impairment. The inter-related interactions and synergistic properties among its related nutritive factors (i.e. fatty acid composition, glycemic load, micronutrient density, macronutrient density, fibre content) are postulated to promote biological risk factors (e.g. increased AGES, ROS, reduced mitochondria function and synthesis), which, in turn, exacerbate potential pathophysiologic deficits in crucial brain areas, including the hippocampus and the PFC. Ultimately, as a consequence of such aversive pathway, there is an increased likelihood of accelerated age-related cognitive function and a higher risk of neurodegenerative disorders such as dementia and AD. In line with this evidence, it would seem theoretically logical to suggest that older adults from Western countries should be encouraged to adopt a MedDiet pattern in place of a Western diet. However, as highlighted above, strong intrinsic Western socio-cultural values, traditions and norms, together with palatability, availability, and cost may impede on the ability to enforce this proposition among some older Western populations.

As suggested above, perhaps a more “Westernised” MedDiet intervention may potentially be a more feasible approach. Future empirical studies, particularly randomised trials with sufficient power and length of time, that take into account Western socio-cultural factors (e.g. food availability, cost, palatability, food access) with the association between the MedDiet and age-related cognitive function will be needed to better demonstrate whether or not the above conjectures are not only valid but also feasible. This type of empirical conduct seems to be greatly lacking among the body of studies reviewed for this paper, and in the area in general. It will be extremely important to address in future research, given a statistically significant finding does not necessarily mean that the intervention will be meaningful or feasible in the real-world. Indeed, decisions made from external Government bodies, medical practitioners and health care workers on the feasibility of interventions such as the MedDiet for Western populations will need this type of comprehensive evidence before they can consider developing them further into real-world policies and practices.

In addition, while the present review is primarily focused on whether prevention of cognitive decline can be achieved in Western older populations through means of dietary modification (i.e. MedDiet), it may be worthwhile for future RCTs to explore the possibility of investigating a multifactorial approach to prevention. For example, examining whether a MedDiet intervention (either traditional or “Westernised”) in combination with other postulated factors such as physical activity, smoking, cognitive exercise/activity, and social engagement (Williams and Kemper, 2010) has the same or greater effect on the ageing brain than simply a diet-alone intervention. Indeed, recent meta-analyses in the area (Blondell et al., 2014; Beydoun et al., 2014) have shown that older adults with higher levels of physical activity are at a reduced risk for cognitive decline and dementia when compared to those with lower levels of physical activity. Similarly, pooled results from Anstey et al. (2007) meta-analysis indicated that compared with non-smokers, elderly smokers had an increased risk of AD, and an increased decline in cognitive performance.

In summary, the findings from this review may be most relevant to those older adults with strong adherence to the Western diet who are contemplating ways to preserve their cognitive health. It has also contributed to the literature by demonstrating that while there is a convincing level of evidence from principal studies in the area attesting to the postulation that a MedDiet, over a Western diet, may be beneficial in preserving age-related cognitive function, there remains the need for longer term, larger scale dietary intervention trials to confidently establish that the MedDiet can be a long-term and feasible preventative approach for older adults in Western countries.

Competing interests

The authors wish to declare they have no competing interests.


Synaptic plasticity and cognition in middle-aged rats. Hippocampus 18 (11), 1085–1098.


