

## Selective Diets for Dementia Disorders

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### Abstract

The global incidence of Alzheimer's disease (AD) is ever-increasing and all current therapies, when effective, remain only symptomatic. Diet, including fruit and vegetable juicing, nutritional supplements, and ketogenic supplements have been found to improve the condition of subjects presenting neurodegenerative disorders. Under various conditions, it is becoming increasingly evident that a Mediterranean-type diet supplemented by olive oil and several different forms of physical exercise may improve global cognition. This type of selective diet that has been combined to be augmented by olive oil and soy isoflavone supplements is linked to potential improve memory and learning, as well as several other necessary daily activities, and several biomarkers of brain health and function. There is an ever-growing trend towards guidelines promoting a greater consumption of plant food-based dietary patterns combined with limitations upon the consumption of animal-based food and a plethora of more-or-less specific guidelines have been formulated. Individual-centered strategies that combine interventions to improve physical, cognitive, and psychosocial functioning may offer improvements to lifestyle (e.g., change in diet) that promote cognitive health in the oldest-old.

**Keywords:** Diet selection; Vegetables; Meats; Supplements; Lifestyle; Cognition; Dementia

### Dementia Disorders

Alzheimer's disease (AD) and other dementia conditions present a neurodegenerative panglial-neuronal disorder with long-standing brain hypometabolism, aberrations in both neuronal and astrocytic glucose metabolism, in lammation, hyperexcitability, and various types of dementia. he global incidence of AD is ever-increasing and all current therapies, when effective, remain only symptomatic. Lifestyle alterations seem to be a necessary ingredient of any therapy. For example, several disparities arising from sociodemographic evidence, including income inequality, and targeting interventions to improve depressive symptoms and vascular risk factors, including diabetes, may play an important role in preserving cognition among women who survive to 80+ years of age. Cognitive decline or dementia is a debilitating problem of neurological disorder. It has been considered for quite some time that the so-called "Mediterranean diet" holds particular advantages for healthy brain aging [1-4], through preserved structural connectivity in older subjects [5], preservation of cognitive integrity [6] and actions against metabolic diverse disorders including cancer, pulmonary disease and cognition defects [7]. Another aspect of this type of diet is expressed by date palm fruits which offer a reliable source of dietary fiber and are rich in total phenolics and natural antioxidants, such as anthocyanins, ferulic acid, protocatechuic acid and caffeic acid, all compounds providing a range of neuroprotective benefits. he APPsw/Tg2576 mouse model of AD displays age-related deterioration in cognitive performance as well as amyloid-beta (A $\beta$ ) accumulation, and this laboratory preparation therefore offers an

effective animal model for examining different mechanisms of accelerated brain aging and senescence through the perspectives of multiple biomarkers. In standard diet-fed transgenic APPsw]/Tg2576 mice marked cognitive impairments, increased anxiety-related behavior, and severe impairment in spatial learning ability, position discrimination learning ability and motor coordination were displayed in comparisons with wild-type on the same diet. Transgenic APPsw]/Tg2576 mice fed 2% and 4% date supplementation at the age of 18 months evidenced lower levels of both A $\beta$  proteins in those date fruits supplemented groups than those mice without the diet supplement [8]. The neuroprotective advantages offered by the 4% date fruit-diet given to AD mice were markedly higher than 2% date fruit-diet supplementation. Curative treatment posits a major lacuna. Naringin and rutin represent a pair of dietary flavonoids that are natural flavonoid agents that are known to induce pleiotropic-type neuropharmacological effects with potential neuroprotective benefits. Their study evaluated these flavonoids for their potential to improve the most common form of episodic memory (memory of autobiographical events in relation to time, places etc.) in different, yet parallel, animal models assessing short-term and long-term memory, respectively.

Adequate nutrition and physical exercise interventions provide the two potential lifestyle modifiable factors that have accumulated considerable and focal interest for their potential in the prevention or management of this challenging disease [9,10], with proper diet for the elderly as a modifiable risk factor [11]. The integration of longitudinal/semi-longitudinal epidemiological data combined with biomarkers of disease, including brain imaging and morphological studies, and randomized controlled interventions are presenting further insights into progressive and subtle neurological changes associated with

dietary factors in individuals at risk for or living with AD. Neuro-imaging techniques have been utilized to examine the effects on brain functional parameters and neuroanatomy, and assess the effects of dietary supplementations and nutritional patterns in relation to neurodegeneration and AD-related features [12]. Several dietary supplements have offered more-or-less promising benefits as observed both in the clinical reality and in the animal laboratory, including docosahexaenoic acid (DHA) [13], low-fat with metformin supplementation [14], moderate levels of seafood consumption [15], hazelnut (*Corylus avellana L.*) dietary supplement [16], creatine supplementation [17], ketogenic diet [18], dietary coconut which comprises medium-chain fatty-acids that may be converted to ketones easily [19], flavanols that are highly represented in cocoa extracts [20], and linalool which occurs in many natural oils [21]; all these potential dietary ingredients may either delay AD onset or even reverse its progress after symptoms have made their debut. An improved understanding of mechanisms involved in nutritional influences on AD risk and progression, such as oxidative stress and loss of neuronal membrane integrity, as well as the presence of associated disorders, including diabetes, obesity and metabolic syndrome [22], has offered a wider range and availability of interventional strategies. Berti et al. [23] have described how specific dietary nutrient patterns are associated with brain biomarkers of AD in cognitively normal individuals, suggesting that dietary interventions may exert a role in the prevention of AD by modulating AD-risk through its effects on A $\beta$  and associated neuronal impairment. Thus, the identified 'AD-protective' nutrient combination was linked to higher intakes of fresh fruit and vegetables, whole grains, fish and low-fat dairies, accompanied by lower intake of sweets, fried potatoes, high-fat dairies, processed meat and butter.

Madhavadas et al. [24] found that the supplementation of 'dark-chocolate' reduced the hyperglycemia, inhibited the cholinesterase activity in the hippocampal tissue homogenates, and improved the cognitive performance in spatial memory-related Barnes maze task in aged rats. Increases in the cell volumes of neurons in the CA3 region of the hippocampus of the supplemented rats were obtained that accompanied the benefits of enhanced cognitive function, hippocampal cholinergic activity and corrections for metabolic disruptions. Furthermore, nutritional interventions that utilize anti-inflammatory nutrients, e.g. cloves, ginger, rosemary, turmeric, etc, may be used to treat type-2 diabetes, cardiovascular disorders and obesity, that may or may not be implicated in AD [25]. Hosono et al. [26] have observed that a four-month dietary treatment of Tg2576 mice, that have a normal development but exhibit age-related cognitive impairments, with an arachidonic acid- or a docosahexaenoic acid-containing diet prevented expressions memory impairment at 13 months-of-age through the alteration of amyloid- $\beta$  protein precursor (A $\beta$ PP) processing (see also Hosono et al. [27] Teng et al. [28]). There is a great variation in the availability of dietary supplements: Huperzine A, which is available as a dietary supplement in the United States, is an example of an acetylcholinesterase inhibitor extracted from *Huperzia Serrata*, a firmoss, which has been applicable for a wide range of diseases in traditional Chinese medicine for fever and neuro-inflammatory infections. The potential dietary supplement induces its protective effects mainly via  $\alpha$ 7nAChRs and  $\alpha$ 4 $\beta$ 2nAChRs, thereby producing a potent anti-inflammatory response by decreasing IL-1 $\beta$ , TNF- $\alpha$  protein expression, and suppressing transcriptional activation of NF- $\kappa$ B signaling [29]. Yamakawa et al. [30] studied the effects of anthocyanoside extracts (*Vaccinium myrtillus* anthocyanoside (VMA)), occurring in all tissues of higher plants, obtained from bilberry on the *in vitro* progression of A $\beta$  fibril formation with the *in*

*in vivo* effects of this compound on AD pathogenesis; they belong to a putatively 'parent' class of 'stem' molecules, the flavonoids. The treatment diet containing 1% *Vaccinium myrtillus* anthocyanoside prevented the cognitive degeneration accompanied by an increased aggregate deposition of insoluble deposits in AD mice compared with mice raised on a control diet. Stress induced within metabolic processes within laboratory environments through recourse to a high-fat diet combined low-dose injection of streptozotocin (exposure to nitrosamine) before the appearance of senile plaques and cardiovascular-related neuro-inflammatory outbursts in APP/PS1 transgenic mice [31,32]. Yeh et al. [33] found that streptozotocin-induced peripheral metabolic stress contributed to vascular inflammation and astrocyte reactivity in the parenchyma and may impair activity of daily living skill and cerebral glucose metabolism in APP/PS1 mice. Diets that retain anti-inflammatory capabilities of regulating the synthesis and activity of inducible nitric oxide synthase under high-glucose levels, such as a glabridin supplement, may offer an anti-inflammatory protective agency in diabetes-related vascular dysfunction and disorders linked to AD [34]. Finally, it has been shown that markedly enhanced levels of cytokines linked to pro-inflammation, IL-1 $\beta$ , IL-2, IL-3, IL-4, IL-5, IL-6, IL-9, IL-10, TNF- $\alpha$  and Eotaxin activity, were reduced through the dispensation of an array of dietary supplements/food composed from pomegranates, figs, or dates to transgenic APPsw/Tg2576 mice [35]. Furthermore, putative delays in the formation of senile plaques, as indicated by a decreasing tendency of brain A $\beta$ 1-40 and A $\beta$ 1-42 contents, were observed in these laboratory mice.

## Conclusion

The prevailing trend for cognitive-behavioral and neural longevity continues towards diets based upon vegetable-fruit produce rather than meat produce. Remarkably however, the dietary patterns selected and characterized by the alternate Mediterranean diet score, the Healthy Eating Index-2010, the Alternate Healthy Eating Index 2010, or the Dietary Approach to Stop Hypertension dietary scores were observed not to be linked with cognitive decline observed in older women that were investigated for over several-year periods [36]. Adherence to a healthy dietary pattern did not modify the risk for cognitive decline in women with hypertension. While this result does not necessarily confound the essential role of diet in aging, it does imply that a greater stringency in decisions regarding 'appropriate' or 'inappropriate' diets is warranted. In this context, one provocative question is whether or not one may facilitate and empower individuals to make self-directed choices to improve their diet. For instance, maladaptive behavior or destructive coping strategies (e.g., lack of physical exercise, smoking and drinking), may alter bodily functions that can have a significant impact on structural integrity of the body, for example, obesity or inactiveness resulting in cardiovascular diseases or type II diabetes [37]. This type of maladaptive behavior is related to, besides genetic factors, the person's inability to make self-directed choices with regard to her/his health show that individual differences in personality, lifestyle, and stress account for large prevalence of mortality from physical disorders in the USA). Fortunately, person-centered approaches that combine interventions to improve physical, cognitive, and psychosocial functioning promote sustainable personality development [38]. In other words, biopsychosocial interventions are needed in order to motivate individuals to choose an appropriate diet.

## Conflict of Interest

Dr. Danilo Garcia is the Director of the Blekinge Center of Competence, which is the Blekinge County Council's research and development unit. The Center works on innovations in public health and practice through interdisciplinary scientific research, person-centered methods, community projects, and the dissemination of knowledge in order to increase the quality of life of the habitants of the county of Blekinge, Sweden.

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