

# POST-PRANDIAL DYSMETABOLISM AND THE VASCULAR COGNITIVE DECLINE

Corina ZORILĂ

“Vasile Goldis” Western University Arad, România

**ABSTRACT.** Preventing or postponing the onset of cognitive decline and delaying or slowing its progression would lead to a consequent improvement of health status and quality of life in older age. The diet is considered an important factor of a healthy state but there are debates about what the diet must to cover. Dietary and lifestyle factors play also a central role in the etiology of post-prandial dysmetabolism. Since several dietary factors affect the risk of cardiovascular disease, it can be assumed that they also influence the risk of dementia. Promising non-pharmacologic approaches to the normalization of post-prandial dysmetabolism are evolving. The traditional Mediterranean diet, which is rich in minimally processed natural foods, low in caloric density but high in nutrient density, have been associated with improved CV health and even with the limitation of cognitive decline. We examine the possible role of macronutrients and food nutrients, with a particular focus on the Mediterranean diet in modulating the risk of Alzheimer disease and dementia.

**Keywords:** dementia, Mediterranean diet, oxidative stress

---

## INTRODUCTION

Preventing or postponing the onset of cognitive decline and delaying or slowing its progression would lead to a consequent improvement of health status and quality of life in older age. The causes of dementia and predementia syndromes are unknown; however, some studies have suggested that it may be preventable (Panza F. Mediterranean diet and cognitive decline; Peters R. The prevention of dementia) The World Alzheimer Report 2011 shows that there are interventions that are effective in the early stages of dementia, some of which may be more effective when are started earlier (The World Alzheimer Report 2011). There are a large number of conditions which cause the symptoms of dementia, as a result of changes that happen on the brain and the ultimate loss of nerve cells (neurons). The most common diseases associated with dementia are: Alzheimer's disease (AD), vascular dementia, dementia with Lewy bodies, fronto-temporal dementia, but Alzheimer's disease and vascular dementia are responsible for up to 90% of cases of dementia. The vascular and related factors that have been associated with dementia and cognitive decline include hypertension and elevated blood pressure, total cholesterol, diabetes mellitus, the metabolic syndrome (Anstey K.J. Cholesterol as a risk factor for dementia and cognitive decline: a systematic review of prospective studies with meta-analysis; Qiu C. The age-dependent relation of blood pressure to cognitive function and dementia; Luchsinger J. A. Adiposity, Type 2 diabetes, and Alzheimer's disease.)

Drugs currently used for the treatment of cognitive decline produce limited clinical benefit and do not treat the underlying causes of the disease. In these conditions, it seems reasonable to search for other types of therapy. The diet is considered an important factor for a healthy state and for the diseases' prevention, but there are debates about the composition of the diet in such circumstances.

Some studies show that elevated saturated fatty acids could have negative effects on age-related cognitive decline and mild cognitive impairment (MCI). Furthermore, at present, epidemiological evidence suggests a possible association between fish consumption, the level of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA); in particular, n-3 PUFA and a reduced risk of cognitive decline and dementia (Solfrizzi V. Dietary fatty acids in dementia and predementia syndromes: epidemiological evidence and possible underlying mechanisms).

Deficiencies of some micronutrients (especially vitamins B1, B2, B6, B12, C and folate) have been described quite frequently in elderly people and found to be significantly associated with MCI (Solfrizzi V. Dietary fatty acids in dementia and predementia syndromes: epidemiological evidence and possible underlying mechanisms; Parrott M.D. Dietary influences on cognitive function with aging. From high-fat diets to healthful eating.) Poorer cognitive function and an increased risk of vascular dementia were found to be associated with a lower consumption of some dietary products as milk or dairy products. However, the consumption of whole-fat dairy products may be associated with cognitive decline in the elderly (Luchsinger J.A. Diet and Alzheimer's disease.).

Light-to-moderate alcohol use may be associated with a reduced risk of incident dementia and AD, while for vascular dementia, cognitive decline and predementia syndromes, the current evidence is only suggestive of a protective effect (Peters R. Alcohol, dementia and cognitive decline in the elderly. a systematic review.).

The exaggerated supraphysiological post-prandial spikes in blood glucose and blood lipids are called post-prandial dysmetabolism. This state can generate excess free radicals that trigger a biochemical cascade resulting in: inflammation, endothelial dysfunction and sympathetic hyperactivity. Systemic inflammation is increasingly recognized as an important mediator of coronary artery disease (CAD) and other common chronic degenerative diseases such as diabetes and Alzheimer dementia (Frisardi V. Metabolic-cognitive syndrome: a cross-talk between metabolic syndrome and Alzheimer's disease.). These post-prandial changes when repeated multiple times daily might cause lead to atherosclerotic lesions and CAD.

Dietary and lifestyle factors play also a central role in the etiology of post-prandial dysmetabolism. Recent studies of healthy individuals indicate that a single meal high in saturated fat will cause immediate increases in triglycerides levels, oxidative stress and inflammation, which will conduct to corresponding post-meal worsening of endothelial dysfunction, vasoconstriction and systolic blood pressure (O'Keefe J.H. Dietary Strategies for Improving Post-Prandial Glucose, Lipids, Inflammation, and Cardiovascular Health).

Post-prandial hyperlipemia, manifest as elevated levels of triglycerides, chylomicrons, and remnant lipoproteins, causes oxidative stress and inflammation, and independently, potentates the adverse effects of postprandial hyperglycemia (Hulea St. Vitamins Minerals and Oxidative Stress). The elevated and protracted post-meal lipid levels are common manifestations of insulin resistance and of the metabolic syndrome. Triglycerides are traditionally measured in the fasting state, typically the lowest triglyceride level of the day, so that the post-prandial hyperlipemia is often neglected. Post-prandial triglyceride levels are directly related to angiographic progression of coronary and carotid atherosclerosis. Subanalyses of 3 randomized trials showed that lowering levels of elevated triglycerides by 20% to 40% reduced CAD rates by approximately 30% to 40% (O'Keefe J. The post-prandial hyperglycemia/hyperlipemia hypothesis: a hidden cardiovascular risk factor?).

There are increasing evidences for an independent association between hypertriglyceridemia and cardiovascular disease by new guidelines that identify non-high-density lipoprotein cholesterol (HDL-C) as a secondary target for therapy in patients with elevated triglyceride (O'Riordan M. Fish Oil Added to Statin Therapy Reduces Risk For Major Coronary Events). This association is probably related to the atherogenicity of some species of TG-rich lipoproteins, particularly small very-low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL) particles (Hulea St. Vitamins Minerals and Oxidative Stress; O'Keefe J. The post-prandial hyperglycemia/hyperlipemia hypothesis: a hidden cardiovascular risk factor?). The high level of postprandial triglycerides is accompanied by high level of CRP and the residual risk for subsequent vascular disease events remains high. Other therapeutic strategies are, beyond attainment of the LDL-C target goal, to reduce non-high-density lipoprotein-cholesterol (non-HDL-C), respective the level of TG. Since several dietary factors affect the risk of cardiovascular disease, it can be assumed that they also influence the risk of dementia.

## OXIDATIVE STRESS

Excessive ingestion of calorie-dense, easily digestible food causes abnormal rises in blood glucose and triglyceride levels. This bolus of energetic substrate overwhelms the metabolic capabilities of the mitochondria in the over nourished muscle and adipose tissues. Glucose and free fatty acids flood the Krebs cycle, stimulating an excess of the reduced form of nicotinamide adenine dinucleotide production, which outstrips the capacity of oxidative phosphorylation and drives the transfer of single electrons to oxygen, creating free radicals such as superoxide anion. The transient increase in free radicals acutely triggers atherogenic changes including inflammation, endothelial dysfunction, hypercoagulability, and sympathetic hyperactivity. This oxidative mechanism also contributes to the progression of vascular lesions.

## NON-PHARMACOLOGIC THERAPIES FOR POST-PRANDIAL DYSMETABOLISM

Promising non-pharmacologic approaches to the normalization of post-prandial dysmetabolism are evolving. The typical dietary pattern of Mediterranean Diet Model is characterized by a:

- high intake of vegetables, fruits and nuts, legumes, cereals,
- fish and monounsaturated fatty acids in larger quantities (MUFA);
- relatively low intakes of meat and dairy products;
- moderate consumption of alcohol (wine).

Only recently, higher adherence to a Mediterranean-type diet was associated with decreased cognitive decline, although the Mediterranean diet combines several fresh foods, micro- and macro-nutrients already separately proposed as potential protective factors against dementia and predementia syndromes (Scarmeas N. Mediterranean diet and risk for Alzheimer's disease; Bjelakovic G. Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention: Systematic Review and Meta-Analysis).

Higher levels of consumption of olive oil, very rich in MUFA, are considered the hallmark of the traditional Mediterranean-type diet, and some recent studies have suggested that dietary fatty acids, particularly high MUFA intake and regular fish and n-3 polyunsaturated fatty acid (PUFA) consumption, may play a role in the prevention of cognitive decline associated with aging or dementia (Solfrizzi V. Dietary fatty acids intake: possible role in cognitive decline and dementia; Assisi A. Fish oil and mental health. the role of n-3 long-chain polyunsaturated fatty acids in cognitive

development and neurological disorders; Cunnane S.C. Fish, docosahexaenoic acid and Alzheimer's disease; Solfrizzi V. Dietary fatty acids in dementia and predementia syndromes: epidemiological evidence and possible underlying mechanisms). Omega-3 fatty acids or fish oils are essential fatty acids that are thought to inhibit VLDL and TG synthesis in the liver. Omega-3 fatty acids have been shown to significantly reduce TG levels and increase LDL-C levels in patients with high TG. Elevated dietary MUFA and PUFA n-3 and high fish consumption, alongside high levels of antioxidants from fruit and vegetables (Dai Q. Fruit and vegetable juices and Alzheimer's disease. The Kame project), and moderate alcohol consumption (Parrott M. D. Dietary influences on cognitive function with aging. From high-fat diets to healthful eating) may have a beneficial effect on the risk of dementia. Japan EPA Lipid Intervention Study (JELIS) show the addition of eicosapentaenoic acid (EPA) to the diet significantly reduced the incidence of major coronary events. This fact can be attributed to the improvement of vascular status, with endothelial benefits, triglyceride-lowering, and anti-inflammatory effects.

## THE DIET AND THE INFLAMMATION

Specifically, a diet high in minimally processed, high-fiber, plant-based foods such as vegetables and fruits, whole grains, legumes, and nuts will markedly blunt the post-meal increase in glucose, triglycerides, and inflammation.

Low glycemic index vegetables and fruits, nuts, lean protein, vinegar, tea, fish oil, calorie restriction, weight loss, each significantly improve post-meal inflammation.

Cinnamon is a calorie-free herb rich in antioxidants that, when added to a high-glycemic-index meal, significantly reduces the post-prandial glucose excursion, partly by slowing gastric emptying.

This anti-inflammatory diet should be considered for the primary and secondary prevention of coronary artery disease and vascular dementia.

Dietary antioxidants such as those present in deeply pigmented plant-based foods and drinks such as berries, red wine, dark chocolate, tea, help to protect the vascular endothelium from post-prandial oxidant stress and inflammation independently of their effects on post-prandial glucose and triglyceride levels.

Most lipophilic antioxidants, such as the hydrocarbon carotenoids (beta-carotene, alpha-carotene and lycopene), decreased most LDL level, followed by the less lipophilic oxygenated carotenoids (lutein/zeaxanthin and beta-cryptoxanthin) and the tocopherols. Flavonoids can have anti-inflammatory and antiplatelet effects. Quercetin may be the mechanisms whereby red wine appears to produce benefit on CV events (Zorila Corina, Natural antioxidants today, in vol. Environmental Biodiversity and Health, proceeding of Euroregional Conference).

Small quantities of high glycemic index foods such as white rice, glucose or potatoes will have a proportionally smaller effect on post-prandial glucose spikes than larger quantities of these foods.

At present, there is no curative treatment for dementia and AD, or a therapeutic approach to prevent the conversion of MCI to dementia. However, while for the vascular hypothesis there is clear evidence about the protective role of Mediterranean diet and its nutrients in preventing all cardiovascular conditions linked to dementia. For the other possible mechanisms it is only possible to suggest hypothetical biological pathways, taking into account the results from animal studies. Therefore, the lack of reproducibility in some results and the speculative aspect of the biological pathways presented, suggest caution (Solfrizzi V. Diet and Alzheimer's Disease Risk Factors or Prevention).

Finally we can say that post-prandial dysmetabolism is an independent predictor of future vascular dementia and Alzheimer disease. Improvements in diet exert profound and immediate favorable changes in the post-prandial dysmetabolism. Based on the current evidence concerning these factors, no definitive dietary recommendations are possible.

## REFERENCES

- Panza F, Solfrizzi V, Colacicco AM et al. Mediterranean diet and cognitive decline. *Public Health Nutr.* 7(7), 2004, 959–963.
- Peters R. The prevention of dementia. *Int. J. Geriatr. Psychiatry* 24(5), 2009, 452–458
- The World Alzheimer Report 2011
- Anstey KJ, Lipnicki DM, Low LF. Cholesterol as a risk factor for dementia and cognitive decline: a systematic review of prospective studies with meta-analysis. *Am. J. Geriatr. Psychiatry.* 16(5), 2008, 343–354
- Qiu C, Winblad B, Fratiglioni L. The age-dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurol.* 4(8), 2005, 487–499
- Luchsinger JA, Gustafson DR. Adiposity, Type 2 diabetes, and Alzheimer's disease. *J. Alzheimers Dis.* 16(4), 2009, 693–704
- Solfrizzi V, Frisardi V, Capurso C et al. Dietary fatty acids in dementia and predementia syndromes: epidemiological evidence and possible underlying mechanisms. *Ageing Res. Rev.* 9(2), 2010, 184–199
- Parrott MD, Greenwood CE. Dietary influences on cognitive function with aging. From high-fat diets to healthful eating. *Ann. NY Acad. Sci.* 1114, 2007, 389–397
- Luchsinger JA, Noble JM, Scarmeas N. Diet and Alzheimer's disease. *Curr. Neurol. Neurosci. Rep.* 7(5), 2007, 366–372
- Peters R, Peters J, Warner J, Beckett N, Bulpitt C. Alcohol, dementia and cognitive decline in the elderly. a systematic review. *Age Ageing* 37(5), 2008, 505–512

- Frisardi V, Solfrizzi V, Seripa D et al. Metabolic-cognitive syndrome: a cross-talk between metabolic syndrome and Alzheimer's disease. *Ageing Res. Rev.* 9(4), 2010,399–417
- O'Keefe J.H; Gheewala N.M, O'Keefe J.O., Dietary Strategies for Improving Post-Prandial Glucose, Lipids, Inflammation, and Cardiovascular Health, *J Am Coll Cardiol.* 2008;51-3
- Hulea St, Vitamins Minerals and Oxidative Stress, Ed. SUniversal-Publishers, Boca Raton Florida USA, 2008
- Mellen P, Cefalu W, Herrington D. Diabetes, the metabolic syndrome, and angiographic progression of coronary artery disease in postmenopausal women. *Arterioscler Thromb Vasc Biol* 2006, 26: 189–93.
- O'Keefe J, Bell D. The post-prandial hyperglycemia/hyperlipemia hypothesis: a hidden cardiovascular risk factor? *Am J Cardiol* 2007; 100:899 –904
- O'Riordan M. Fish Oil Added to Statin Therapy Reduces Risk For Major Coronary Events. *Lancet* 2007;369:1062-1063, 1090-1098
- Scarmeas N, Stern Y, Tang MX, Mayeux R, Luchsinger JA. Mediterranean diet and risk for Alzheimer's disease. *Ann. Neurol.* 59(6), 2006, 912–921
- O'Keefe H.J, Gheewala N.M, Joan O'Keefe, Dietary Strategies for Improving Post-Prandial Glucose, Lipids, Inflammation, and Cardiovascular Health , *J. Am. Coll. Cardiology*, 2008, 51(3)
- Stevenson E, Williams C, Mash L, Phillips B, et al. Influence of high-carbohydrate mixed meals with different glycemic indexes on substrate utilization during subsequent exercise in women. *Am J Nutr* 2006; 84:354–60.
- Byrans JA, Judd PA, Ellis PR. The effect of consuming instant black tea on postprandial plasma glucose and insulin concentrations in healthy humans. *J Am Coll Nutr* 2007;26:471–7
- Solfrizzi V, D'Introno A, Colacicco AM et al. Dietary fatty acids intake: possible role in cognitive decline and dementia. *Exp. Gerontol.* 40(4), 257–270 (2005)
- Assisi A, Banzi R, Buonocore C et al. Fish oil and mental health. the role of n-3 long-chain polyunsaturated fatty acids in cognitive development and neurological disorders. *Int. Clin. Psychopharmacol.* 21(6), 319–336 (2006).
- Cunnane SC, Plourde M, Pifferi F, et al. Fish, docosahexaenoic acid and Alzheimer's disease. *Prog. Lipid Res.* 48(5), 239–256 (2009).
- Solfrizzi V, Frisardi V, Capurso C et al. Dietary fatty acids in dementia and predementia syndromes: epidemiological evidence and possible underlying mechanisms. *Ageing Res. Rev.* 9(2), 184–199 (2010).
- Dai Q, Borenstein A, Wu Y, Jackson JC, Larson EB. Fruit and vegetable juices and Alzheimer's disease. the Kame project. *Am. J. Med.* 119(9), 751–759 (2006).
- Parrott MD, Greenwood CE. Dietary influences on cognitive function with aging. From high-fat diets to healthful eating. *Ann. NY Acad. Sci.* 1114, 389–397 (2007).
- Zorila Corina, Natural antioxidants today, in vol. *Environmental Biodiversity and Health*, proceeding of Euroregional Conference, May 11-13, 2007 Arad, Ed.“V. Goldis University Press,”p. 236-238,
- Bjelakovic G., Nikolova D., Gluud L., at al, Mortality in Randomized Trials of Antioxidant Supplements for Primary and Secondary Prevention: Systematic Review and Meta-Analysis, *Medscape Family Medicine*, Posted 03/27/2007
- Solfrizzi V.,s Panza F., Frisardi V., et al, Diet and Alzheimer's Disease Risk Factors or Prevention, *Expert Rev Neurother.*2011; 11(5):677-708