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## Expert report

# Cognitive Decline, Alzheimer's and Parkinson's Diseases — does dietary pattern play a role?

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## Contents

1	Demographic trends	2
2	What is the role of dietary pattern?	3
3	Coffee	3
4	Coffee and Alzheimer's Disease	4
5	Coffee and Parkinson's Disease	4
6	Possible mechanisms — coffee in relation to AD and PD	5
7	Conclusion	6
8	Key takeaways	7
9	About ISIC	8
10	References	9





## Demographic trends

For the first time in history, most people can expect to live into their 60s and beyond<sup>1,2</sup>. In higher-income regions the proportion of people aged over 80 years is projected to more than double until 2100, reaching nearly 15 per cent of the population<sup>1,2</sup>. The majority of older adults are in good health and live independent and active lives. Maintenance of independence as long as possible is therefore also strictly a priority for well-being and self-perception in this part of the population. However, with increasing age, the risk of disease and disabilities increases. Neurodegenerative conditions such as Alzheimer's (AD) and Parkinson's Diseases (PD) are two distinct examples of conditions developing in later years with profound effect on independence, well-being and self-perception<sup>3</sup>.

The number affected with AD is estimated to increase globally from today's 47 million to 75 million 2030 and to 132 million in 2050<sup>3</sup>. PD is the second most common age-related neurodegenerative disorder after AD. Globally approximately 7 million people are affected<sup>4</sup>. The incidence rate rises from 1 per cent in those over 60 years of age to 4 per cent of the population over 80, more often affecting males than females<sup>4</sup>.

Strong interconnected pathologies between life-style related conditions as diabetes, obesity, insulin resistance, and cardiovascular disease and AD<sup>5</sup> and PD<sup>6</sup> have been demonstrated, indicating that lifestyle might be an important part of the risk. This report aims to give an overview of the growing body of research in the field of diet and cognitive decline with focus on AD and PD.

### Alzheimer's Disease estimated global increase



**Today**  
**47 million**  
**2030**  
**75 million**  
**2050**  
**132 million**

### Parkinson's Disease population incidence rate rises

**1%**   
**in those over  
60 years of age**  
**4%**   
**in those over  
80 years of age**<sup>4</sup>



## What is the role of dietary pattern?

Nutrition research today focuses more on the synergistic effects of a dietary pattern, rather than on particular nutrients or food items in maintaining good health<sup>5-9</sup>. Probably the most well documented dietary pattern is the Mediterranean<sup>5,8-18</sup>. This diet is characterised by a variety of plant-based foods including fruit, vegetables, seeds, grains and olive oil, and low in saturated fats, animal-derived proteins, and refined sugars. Its antioxidant and anti-inflammatory potential seems beneficial in prevention of several life-style related conditions as insulin resistance, type 2 diabetes, cardiovascular disease, stroke and cancer<sup>5,10</sup>.

Positive associations between Mediterranean dietary patterns — where the focus is on plant based foods (e.g. DASH diet, MIND diet, anti-inflammatory diet) — and better cognitive scores and a lower risk of AD<sup>5,7-16</sup> have been shown. Specific dietary factors present in these diets, such as unsaturated fat, have shown protective effects in PD<sup>6,17</sup>. At the same time, compounds associated with higher PD risk, such as saturated fat, are present in smaller amounts in these diets<sup>18</sup>. Although results vary, a majority of studies suggest that closer adherence to a Mediterranean style diet is associated with a lower risk for cognitive decline<sup>6-17</sup>, probably acting by modifying pathways related to a more general aging process<sup>7</sup>.

## Coffee

Among dietary components coffee/caffeine have been identified as interesting in relation to age related cognitive decline and to neurodegenerative conditions such as AD and PD<sup>19,20</sup>. Research suggests that a lifelong regular intake may have protective effects<sup>21-31</sup>. Coffee naturally contains a variety of compounds including caffeine, antioxidants and bioactive substances. These compounds contribute not only to the unique flavour but also to the physiological effects of coffee positively affecting alertness and concentration<sup>32</sup>. A moderate coffee consumption is typically defined as 3-5 cups per day, based on the European Food Safety Authority's (EFSA) review of caffeine safety<sup>33</sup>.



**“A Mediterranean style diet’s anti-inflammatory potential seems beneficial in prevention of several life-style related conditions<sup>5,10</sup>.”**



## Coffee and Alzheimer's Disease

Research on coffee consumption and AD shows varied results<sup>21–28,34</sup>. Many studies suggest that a lifelong intake of coffee/caffeine is associated with a reduced risk of developing AD<sup>21–25,34</sup>, however others show negative results<sup>26–28</sup>. A review from 2018 suggested that more than 75 per cent of available research supports the opinion that caffeine has a favourable effect against cognitive decline and AD<sup>23</sup>.

A 2010 review suggested that daily intake of 3–5 cups of coffee in middle age may lower the risk of the dementia and AD by about 65 per cent as compared to lower amounts of coffee consumption<sup>24</sup>. A further 2017 review also supports the view that moderate coffee consumption may lower the risk for common neurodegenerative conditions including AD<sup>25</sup>. However, a 2018 meta-analysis suggested that the results do not support an association between coffee consumption and a reduced risk of overall dementia or AD specifically<sup>26</sup>.

## Coffee and Parkinson's Disease

PD is characterized by progressive degradation of the nervous system. Research suggests that a higher intake of coffee and caffeine, up to 5 cups of coffee per day, could act as preventative on risk of developing neurodegenerative conditions including Parkinson's Disease (PD)<sup>29–31, 35,36</sup>. Reports of beneficial effects of caffeine are improved motor activity, through neuroprotection<sup>36–39</sup>.

Epidemiological data from the Nurses' Health Study and the Health Professionals Follow-up Study, in total nearly 116 000 individuals, showed additive interaction between no family history of PD and caffeine in men and between caffeine and physical activity in women<sup>40</sup>.

A recent prospective cohort study suggested that life-long intake of coffee, caffeinated tea, together with moderate alcohol consumption and physical activity, are protective. It also found that coffee specifically is protective against disease progression, cognitive decline and mortality<sup>41</sup>. Another prospective cohort study concluded the number of years of coffee consumption is correlated with a significant increase in age at PD onset<sup>42</sup>. A recent review suggested a sex difference in the potential protective effect of coffee, and tea, with a greater beneficial effect in males with PD<sup>6</sup>. The reason for the smaller effect in females suffering from



**“Research suggests that a higher intake of coffee and caffeine, up to 5 cups of coffee per day, could act as preventative on risk of developing neurodegenerative conditions including Parkinson's Disease**  
29–31, 35,36.”



PD might be explained by postmenopausal oestrogen supplementation hiding the effect of caffeine<sup>6</sup>. However, contradicting results with lower PD risk in both men and women was shown in a large prospective study including almost 305 000 participants<sup>43</sup>.

A further 2010 meta-analysis and systematic review found an inverse association between caffeine consumption and the risk of PD<sup>35</sup>. The cumulative meta-analysis indicated a 25 per cent reduction in PD risk among caffeine consumers with an inverse dose-response relationship between the onset of PD and caffeine intake. No significant heterogeneity between studies was found. Furthermore, it has been suggested that absolute lower levels of caffeine and caffeine metabolite profiles might be promising diagnostic biomarkers for early PD<sup>44</sup>.

## Possible mechanisms — coffee in relation to AD and PD

The mechanisms involved in the positive associations found between caffeine in relation to AD<sup>45-48</sup> and PD<sup>6,34</sup> are not yet well understood. Caffeine is suggested as a non-selective blocker of adenosine receptors and has been linked to basic physical functions as the regulation of heart rate, and neural signalling in the central nervous system (CNS). Since the late 1990s, studies on adenosine receptor antagonists, such as caffeine, have shown a reduction in the physical, cellular and molecular damage caused by neurodegenerative disorders such as AD and PD. By this blocking effect, caffeine might protect against inflammatory damage evolving during disease progression.

Caffeine could promote neuronal survival and reduce neurodegeneration in these areas of the brain<sup>45,46</sup>. In PD specifically, caffeine might contribute to positive effects on the symptomatic treatment without provoking marked impairment in the ability to control movements<sup>39</sup>.

In addition to caffeine, coffee also contains other plant-based compounds such as phytochemicals and polyphenols<sup>9,10</sup>, that might be part of the observed positive effects. One class of phytochemicals present in coffee, tea and cacao is methylxanthines, of which caffeine is the best studied. In some research, effects on neuronal network activity have been shown, promoting sustained cognitive performance and protection of neurons against dysfunction of stroke, AD and PD<sup>45-50</sup>. Other methylxanthines include theobromine and theophylline which may also contribute to the beneficial effects of coffee, tea and cacao on brain health<sup>34,51-53</sup>.

In summary, some studies suggest a positive effect of coffee with better cognitive outcomes<sup>21-25,29-31</sup>, whilst others does not support such an effect<sup>26-28</sup>. Firm conclusions about associations cannot yet be drawn.



## Conclusion

Neurodegenerative conditions such as AD and PD markedly change life conditions by successively impairing functional capacity, with profound effects on independence and well-being. Currently no curative treatment is available, and therefore ways to reduce the risk of developing these conditions or relieve symptoms is laudable. At present research has shown promising results regarding the impact of life-style factors including diet. The Mediterranean diet has been of main interest. There are also some interesting studies regarding coffee consumption suggesting that caffeine is potentially beneficial in preventing AD and PD. However, still it is too early to draw firm conclusions regarding causal relationship between dietary factors and the risk of developing AD and PD. Further research is required including both randomized controlled trials, and prospective cohort studies with long follow-up in humans, and purely mechanistic studies to understand the associations in more detail.



## Key takeaways



Dietary pattern may have an impact on the risk of developing neurodegenerative disorders<sup>5-11</sup>



Mediterranean style diets have been associated with a reduced risk of neurodegenerative conditions<sup>10-18</sup>



Coffee consumption may help reduce the risk of neurodegenerative conditions or relieve symptoms<sup>21-25,29-31</sup>



Considering PD, men might benefit more from coffee consumption than women possibly because oestrogen may compete with caffeine<sup>6</sup>



It is too early to draw firm conclusions regarding causal relationship between dietary factors and risk of developing AD and PD<sup>21-31</sup>



Further research is required for better understanding of the associations<sup>21-31</sup>



## About Elisabet Rothenberg



**Elisabet Rothenberg** is a registered dietitian with a PhD. Currently she has a position as assistant professor at Kristianstad University at department of Food and Meal Science. Her research interest is dietary intake and body composition in ageing. Her thesis concerned energy and nutrient intake, food habits and energy expenditure in 70-year olds in Gothenburg. She is involved in several research projects concerning food and nutrition intake of older adults, is the co-author in several text books of health, disease and nutrition, and a frequently hired lecturer. She has an extensive experience of involvement in guideline committees and in educational activities on different academical levels within the field of malnutrition.

## About ISIC

The Institute for Scientific Information on Coffee (ISIC) is a not-for-profit organization, established in 1990 and devoted to the study and disclosure of science related to "coffee and health." Since 2003 ISIC also supports a pan-European education programme, working in partnership with national coffee associations in nine countries to convey current scientific knowledge on "coffee and health" to health care professionals.

ISIC's activities are focused on:

- the study of scientific matters related to "coffee and health"
- the collection and evaluation of studies and scientific information about "coffee and health"

➤ the support of independent scientific research on "coffee and health"

➤ active dissemination of balanced "coffee and health" scientific research and knowledge to a broad range of stakeholders.

ISIC respects scientific research ethics in all its activities. ISIC's communications are based on sound science and rely on scientific studies derived from peer-reviewed scientific journals and other publications.

ISIC members are six of the major European coffee companies: illycaffè, Jacobs Douwe Egberts, Lavazza, Nestlé, Paulig, and Tchibo.

## About coffeandhealth.org

The website [www.coffeandhealth.org](http://www.coffeandhealth.org) is a science-based resource developed for health care and other professional audiences and provides the latest information and research into coffee, caffeine and health.

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## References

- 1 Eurostat (2019) Population structure and ageing. Available at [https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population\\_structure\\_and\\_ageing](https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population_structure_and_ageing)
- 2 UN (2017) World Population Prospects: The 2017 Revision. Available at <https://www.un.org/development/desa/publications/world-population-prospects-the-2017-revision.html>
- 3 WHO (2015) The Epidemiology and Impact of Dementia. Available at [https://www.who.int/mental\\_health/neurology/dementia/dementia\\_thematicbrief\\_epidemiology.pdf](https://www.who.int/mental_health/neurology/dementia/dementia_thematicbrief_epidemiology.pdf)
- 4 Parkinsons Disease Collaborators (2018) Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*, 17(11):939–953.
- 5 Pistollato F. et al. (2018) Nutritional patterns associated with the maintenance of neurocognitive functions and the risk of dementia and Alzheimer's disease: A focus on human studies. *Pharmacol Res*, 131:32–43.
- 6 Boulos C. et al. (2019) Nutritional Risk Factors, Microbiota and Parkinson's Disease: What Is the Current Evidence. *Nutrients*, 11 (8) pii: E1896.
- 7 Abbatecola A.M. (2018) Dietary patterns and cognition in older persons. *Curr Opin Clin Nutr Metab Care*, 21(1):10–13.
- 8 Solfrizzi V. et al. (2017) Relationships of Dietary Patterns, Foods, and Micro- and Macronutrients with Alzheimer's Disease and Late-Life Cognitive Disorders: A Systematic Review. *J Alzheimers Dis*, 59(3):815–849.
- 9 Fernandez M.J.F. et al. (2019) Food Components with the Potential to be Used in the Therapeutic Approach of Mental Diseases. *Curr Pharm Biotechnol*, 20(2):100–113.
- 10 Roman G.C. et al. (2019) Mediterranean diet: The role of long-chain  $\omega$ -3 fatty acids in fish; polyphenols in fruits, vegetables, cereals, coffee, tea, cacao and wine; probiotics and vitamins in prevention of stroke, age-related cognitive decline, and Alzheimer disease. *Rev Neurol (Paris)*, pii: S0035-3787(19)30773-8.
- 11 Chen X. et al. (2019) Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review. *J Alzheimers Dis*, 67(2):583–619.
- 12 Van den Brink A.C. et al. (2019) The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention. for Neurodegenerative Delay (MIND) Diets Are Associated with Less Cognitive Decline and a Lower Risk of Alzheimer's Disease—A Review. *Adv Nutr*, 10(6):1040–1065.
- 13 Van de Rest O. et al. (2015) Dietary patterns, cognitive decline, and dementia: a systematic review. *Adv Nutr*, 6(2):154–68.
- 14 Petersson S.D., Philippou E. (2016) Mediterranean Diet, Cognitive Function, and Dementia: A Systematic Review of the Evidence. *Adv Nutr*, 7(5):889–904.
- 15 Gardener H., Caunca M.R. (2018) Mediterranean Diet in Preventing Neurodegenerative Diseases. *Curr Nutr Rep*, 7(1):10–20.
- 16 Aridi Y.S. et al. (2017) The Association between the Mediterranean Dietary Pattern and Cognitive Health: A Systematic Review. *Nutrients*, 9(7):piiE674.
- 17 Mohammad-Beigi, H et al. (2019) Oleuropein derivatives from olive fruit extracts reduce—Synuclein fibrillation and oligomer toxicity. *J. Biol. Chem.*, 294, 4215–4232.
- 18 Erro, R et al. (2018) Nutritional habits, risk, and progression of Parkinson disease. *J. Neurol.*, 265, 12–23.
- 19 Santos C. et al. (2010) Caffeine intake and dementia: systematic review and meta-analysis. *J Alzheimers Dis*, 20 Suppl 1:S187–204.
- 20 Arab L. et al. (2013) Epidemiologic Evidence of a Relationship between Tea, Coffee, or Caffeine Consumption and Cognitive Decline. *Adv Nutr*, vol. 4:115–122.
- 21 Haller S. et al. (2018) Impact of Coffee, Wine, and Chocolate Consumption on Cognitive Outcome and MRI Parameters in Old Age. *Nutrients*, 10(10). pii: E1391.
- 22 Wu L. et al. (2017) Coffee intake and the incident risk of cognitive disorders: A dose-response meta-analysis of nine prospective cohort studies. *Clin Nutr*, 36(3):730–736.
- 23 Hussain A. et al. (2018) Caffeine: a potential protective agent against cognitive decline in Alzheimer's disease, *Crit Rev Eukaryotic Gene Expression*, Volume 28 (1):67–72.



- 24 Eskelinen M.H, Kivipelto M. (2010) Caffeine as a protective factor in dementia and Alzheimer's disease. *J Alz Dis*, 20 Suppl 1:S167–74.
- 25 Wierzejska R. (2017). Can coffee consumption lower the risk of Alzheimer's disease and Parkinson's disease? A literature review, *Arch Med Sci*, Volume 13 (3):507–514.
- 26 Larsson S.C., Orsini N. (2018) Coffee Consumption and Risk of Dementia and Alzheimer's Disease: A Dose-response Meta-Analysis of Prospective Studies, *Nutrients*, Volume 10 (10):pii E1501.
- 27 Larsson S.C. et al, 2017. Modifiable pathways in Alzheimer's disease: Mendelian randomisation analysis, *BMJ*, 359:j5375.
- 28 Shirai Y. et al. (2019) Green tea and coffee intake and risk of cognitive decline in older adults: the National Institute for Longevity Sciences, Longitudinal Study of Aging. *Pub Health Nutr*, 23:1–9.
- 29 Hernan M.A. et al. (2002) A meta-analysis of coffee drinking, cigarette smoking, and the risk of Parkinson's disease. *Ann Neurol*, 52:276–84.
- 30 Liu R. et al. (2012) Caffeine intake, smoking, and risk of Parkinson disease in men and women. *Am J Epidemiol*, 175(11):1200–7.
- 31 Qi H. et al. (2014) Dose-response meta-analysis on coffee, tea and caffeine consumption with risk of Parkinson's disease. *Geriatr Gerontol Int*, (2):430–9.
- 32 EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2011) Scientific Opinion on the substantiation of health claims related to caffeine and increased fat oxidation leading to a reduction in body fat mass (ID 735, 1484), increased energy expenditure leading to a reduction in body weight (ID 1487), increased alertness (ID 736, 1101, 1187, 1485, 1491, 2063, 2103) and increased attention (ID 736, 1485, 1491, 2375) pursuant to Article 13(1) of Regulation (EC) No 1924/20061. *EFSA Journal*, 9(4):2054.
- 33 EFSA (2015) Scientific Opinion on the Safety of Caffeine. *EFSA Journal*, 13(5):4102.
- 34 Camandola S. et al. (2019) Impact of Coffee and Cacao Purine Metabolites on Neuroplasticity and Neurodegenerative Disease. *Neurochem Res*, 44(1):214–227.
- 35 Costa J. et al. (2010) Caffeine exposure and the risk of Parkinson's disease: a systematic review and meta-analysis of observational studies. *J Alzheimers Dis*, 20 Suppl 1:S221–38.
- 36 Herden L., Weissert R. (2018) The Impact of Coffee and Caffeine on Multiple Sclerosis Compared to Other Neurodegenerative Diseases. *Front Nutr*, 5:133.
- 37 Kolahdouzan M., Hamadeh M.J. (2017) The neuroprotective effects of caffeine in neurodegenerative diseases. *CNS Neurosci Ther*, 23(4):272–290.
- 38 Fablani C. et al. (2018) A novel pharmacological activity of caffeine in the cholinergic system. *Neuropharmacol*, ;135:464–473.
- 39 Rivera-Oliver M., Diaz-Rios M. (2014) Using caffeine and other adenosine receptor antagonists and agonists as therapeutic tools against neuroprotective diseases: a review. *Life Sci*, 101(1–2):1–9.
- 40 Kim I.Y. (2018) Integration of risk factors for Parkinson disease in 2 large longitudinal cohorts. *Neurol*, 90(19):e1646–e1653.
- 41 Paul K.C. et al. (2019) The association between lifestyle factors and Parkinson's disease progression and mortality. *Mov Disord*, 34(1):58–66.
- 42 Gigante A.F. et al (2018) Chronic coffee consumption and striatal DAT-SPECT findings in Parkinson's disease. *Neurol Sci*, 39(3):551–555.
- 43 Liu R. et al. (2013) Alcohol consumption, types of alcohol, and Parkinson's disease. *PLoS ONE*, 8, e66452.
- 44 Fujimaki M. et al. (2018) Serum caffeine and metabolites are reliable biomarkers of early Parkinson disease, *Neurol*, 90(5):e404–e411.
- 45 Arendash G.W. et al. (2006) Caffeine protects Alzheimer's mice against cognitive impairment and reduces brain  $\beta$ -amyloid production. *Neuroscience*, 142:941–52.
- 46 Arendash G.W. et al. (2009) Caffeine reverses cognitive impairment and decreases brain amyloid- $\beta$  levels in aged Alzheimer's disease mice. *J Alzheimers Dis*, 17:661–80.
- 47 Cao C. et al. (2009) Caffeine suppresses amyloid- levels in plasma and brain of Alzheimer's disease transgenic mice. *J Alzheimers Dis*, 17:681–97.



- 48 Cao C. et al. (2011) Caffeine synergizes with another coffee component to increase plasma GCSF: linkage to cognitive benefits in Alzheimer's mice. *J Alz Dis*, 25(2):323–35.
- 49 Fenu S. & Morelli M. (1998) Motor stimulant effects of caffeine in 6-hydroxydopamine-lesioned rats are dependent on previous stimulation of dopamine receptors: a different role of D1 and D2 receptors. *Eur J Neurosci*, 10:1878–84.
- 50 Madeira M.H. et al. (2017) Having a Coffee Break: The Impact of Caffeine Consumption on Microglia-Mediated Inflammation in Neurodegenerative *Mediators Inflamm*, 2017:4761081.
- 51 Tohda C. et al. (2005) Search for natural products related to regeneration of the neuronal network. *Neurosignals*, 14:34–45.
- 52 Tohda C. et al. (1999) Trigonelline-induced neurite outgrowth in human neuroblastoma SK-N-SH cells. *Biol Pharm Bul*, 22:679–82.
- 53 Onatibia-Astibia A. (2017) Health benefits of methylxanthines in neurodegenerative diseases. *Mol Nutr Food Res*, 61(6): 10.1002/mnfr.201600670.