



coffee&health

from the institute for scientific information on coffee

The good things in life: can coffee consumption reduce the risk of developing Alzheimer's Disease?

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Foreword



The role of nutrition is an emerging area in Alzheimer's research and the potential benefits of drinking coffee, on both a nutritional and a social level, are increasingly being developed.

Cognitive decline is a feature of aging, and although some changes can be expected in all of us, there is some evidence that diet and lifestyle may be related to cognition. In fact epidemiological studies suggest that certain lifestyle factors and nutritional elements, including the consumption of coffee and caffeine, may help to slow age-related cognitive decline seen in the older generation.

At Alzheimer Europe's annual conference, a satellite symposium sponsored by the Institute for Scientific Information on Coffee explored the role nutrition can play in reducing the risk of Alzheimer's Disease. Three expert speakers in this area presented the latest research developments and findings, which are documented in this post conference report.

The findings presented at the symposium are very encouraging and help to develop our understanding of the role nutrition plays in Alzheimer's Disease. Coffee is a very popular beverage enjoyed by millions of people around the world and I'm pleased to know that moderate, lifelong consumption could help to protect against Alzheimer's.



Iva Holmerova

Vice Chairperson of Alzheimer Europe



Third Edition

This summary of research into coffee consumption and Alzheimer's Disease is based on findings presented during a symposium on nutrition and cognitive function, held at Alzheimer Europe in October 2014, and has been updated to include the latest research in this area.

The scale of the disease

Alzheimer's Disease is a degenerative brain disease and the most common form of dementia. Between 60-65 percent of people with dementia suffer from Alzheimer's Disease¹.

Dementia starts in late middle age or in old age and results in progressive memory loss, impaired thinking, disorientation, and changes in personality and mood that can lead, in advanced cases, to a profound decline in cognitive and physical functioning. Alzheimer's Disease slowly and progressively destroys brain cells, particularly in the cerebral cortex. It is characterised by the presence of neurofibrillary tangles and plaques containing beta-amyloid – an amino acid chain most commonly associated with Alzheimer's Disease.

Approximately one person in twenty over the age of 65 suffers from Alzheimer's Disease and by 2025, the number of people in the EU aged over 65 is predicted to rise from 15.4% of the population to 22.4%, which is likely to correlate with a rise in Alzheimer's Disease². Approximately 26 million people suffer from Alzheimer's Disease worldwide².



Reducing the risk of developing Alzheimer's Disease

At present, there is no known cure for Alzheimer's Disease as the death of brain cells during the development of the dementia cannot be halted or reversed. This means that primary prevention is very important as a means of delaying or halting the onset of age-related cognitive decline.

As demonstrated in Figure 1, dementia is the end stage of Alzheimer's³. The clinical stages of Alzheimer's are marked by progressive dementia described as 'very mild', 'mild', 'moderate' and 'severe'. These stages are associated with abundant amyloid plaques (red line), the gradual accumulation of NFTs (blue line) and synaptic and neuronal loss in certain brain regions (green line). Prior to this, there is a preclinical phase of about 10 years, during which there are no symptoms, which provides a window of opportunity to intervene before the onset of Alzheimer's and dementia.

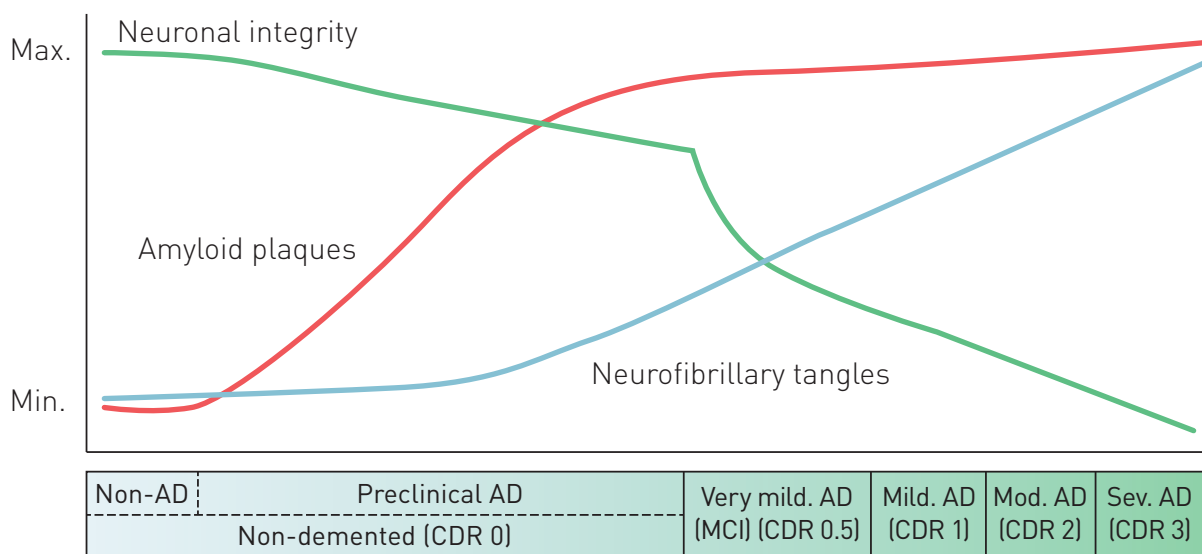
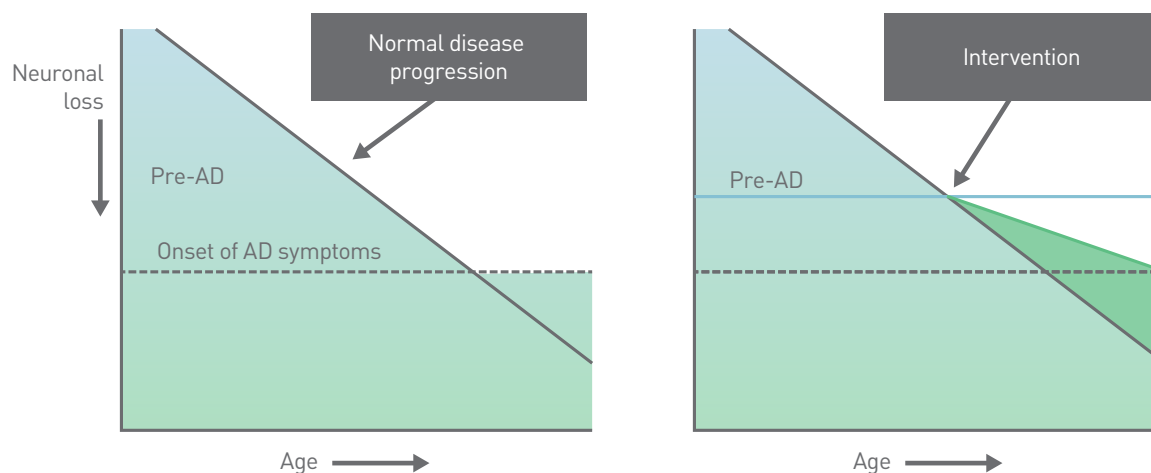


Figure 1: The progression of Alzheimer's Disease from preclinical to clinical stages



Clinical diagnosis of Alzheimer's occurs when the disease is well underway, as symptoms do not become obvious until considerable neurodegeneration has occurred. Figure 2 shows the loss of functional neurons over time that is characteristic of Alzheimer's, with the dotted line demonstrating the onset of symptoms⁴. As illustrated in this figure, if interventions begin pre-symptomatically, the disease may not progress to the point when symptoms become obvious.

Figure 2: Comparison of the progression of Alzheimer's Disease with and without intervention



There is increasing evidence that a holistic approach involving exercise of the body and brain, social interaction and nutrition has an important role in reducing the risk of dementia. With regard to nutrition, epidemiological evidence has suggested that a Mediterranean diet, consisting of fish, fresh fruit and vegetables, olive oil and red wine, is associated with a reduced risk of developing Alzheimer's Disease⁵⁻⁷, a reduced risk for developing Cognitive Impairment⁶ and improve cognition in individuals aged 65 years or older⁸.

Polyphenols

The Mediterranean diet is a complex diet, and research suggests that polyphenols within the diet may offer benefit. Polyphenols are plant metabolites which are found in abundance in the human diet; the richest sources being fruits, vegetables and beverages such as wine, coffee and tea. There are many types of polyphenols, which are broadly split into two categories – flavenoids and non-flavenoids.

Non-flavenoids include phenolic acids such as caffeic acid, found in coffee. Animal studies have shown that rats administered caffeic acid showed improved cognitive function and were protected against aluminium chloride-induced dementia⁹.



Epidemiological evidence on coffee consumption and Alzheimer's

There is an emerging body of literature that looks at coffee consumption and its role in Alzheimer's and dementia. The majority of human epidemiological studies suggest that moderate coffee/caffeine consumption over a lifetime may reduce the risk of developing Alzheimer's, particularly in the elderly¹⁰. Meta-analyses have supported this protective effect¹¹⁻¹³ and research suggests that moderate coffee consumption can reduce the risk of developing Alzheimer's by up to 20%¹⁴, or even 27%¹⁵.

Moderate coffee consumption is typically considered to be 3-5 cups per day.

Short vs. long follow-up

There are two types of epidemiological studies. On the one hand there are those with a short follow-up period, typically 5-10 years, which have consistently shown a significant protective effect of coffee consumption on the development of Alzheimer's Disease¹²⁻¹⁷.

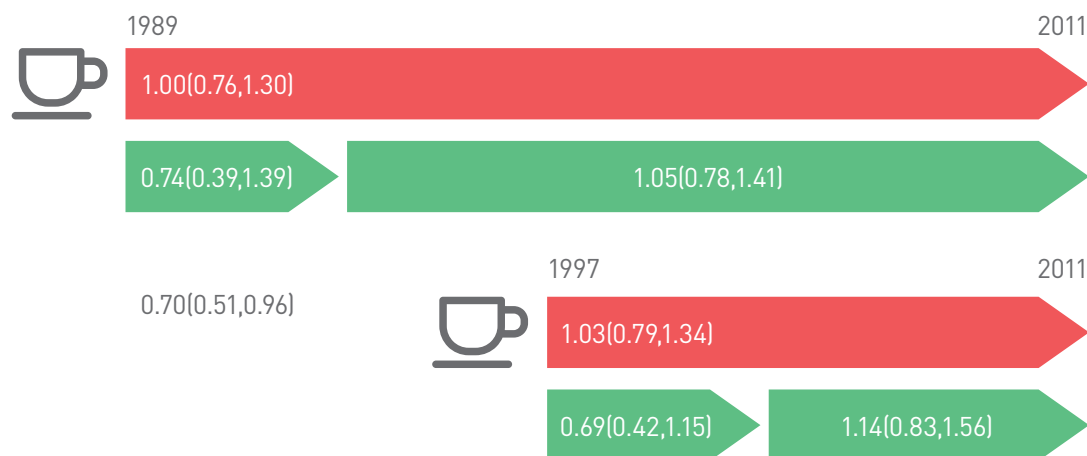
Conversely there are studies with longer follow-up periods of 15 or more years. These have produced less consistent results and researchers have been unable to make firm conclusions about the role of coffee consumption on Alzheimer's Disease¹⁸⁻²¹. A 2015 systematic review highlighted this inconsistency, concluding that larger studies with longer follow-up periods should be encouraged²².

Follow-up to the population-based Rotterdam Study, published in 2014 and funded by the Institute for Scientific Information on Coffee (ISIC), aimed to explore the paradox further. In a population cohort of over 5,000 individuals, the researchers assessed coffee consumption and risk of dementia over both long and short follow-up periods. This was the first study to explore both short and long follow-up in the same population group. The findings showed that coffee consumption has a protective effect on risk of dementia in the short term, however this effect subsided at long term follow-up. The authors concluded that further research was necessary to disentangle the reasons for these findings²³.



Most recently, a meta-analysis published in 2015 has concluded that in the short-term, coffee/caffeine consumption may have a protective effect against Alzheimer's, likely due to its stimulation of the central nervous system; the systematic review also showed a long-term favourable influence in decreasing new incidence Alzheimer's Disease risk²⁴.

Figure 3: Results from short and long follow-up study



Mechanism of coffee consumption and Alzheimer's

Coffee is a very complex beverage containing over 1,000 components. Animal research has investigated which components are responsible for the protective effects of coffee consumption against Alzheimer's, implicating caffeine as the most important component²⁵, as well as polyphenols, such as chlorogenic acids (e.g. caffeic acid, ferulic acid).

Caffeine

Caffeine acts on two hallmarks of Alzheimer's; firstly it reduces the accumulation of beta amyloid peptide, (the protein responsible for the development of amyloid plaques). Secondly, it reduces the hyperphosphorylation of tau protein (the process responsible for the formation of neurofibrillary tangles in Alzheimer's)²⁶. In addition, caffeine reduces inflammation and decreases the extent of neuronal deaths, especially in the hippocampus and cortex regions of the brain involved in memory²⁷. As a neuro-stimulant, caffeine also promotes higher levels of acetylcholine, the neurotransmitter involved in cognition²⁸.



Polyphenols

Polyphenols have high antioxidant properties and play a similar role to caffeine.

A large proportion of our dietary intake of polyphenols comes from coffee²⁹.

These compounds act on the brain to reduce inflammation, reduce neuronal deaths and preserve levels of acetylcholine.

In one study, the polyphenol ferulic acid, found

in coffee, was given to mice in drinking

water³⁰. This was found to protect against

cognitive deficits – mainly spatial and

working memory – and to suppress

inflammation and prevent the

loss of acetylcholine from the

cerebral cortex – all factors

that characterize Alzheimer's

Disease³¹⁻³³.

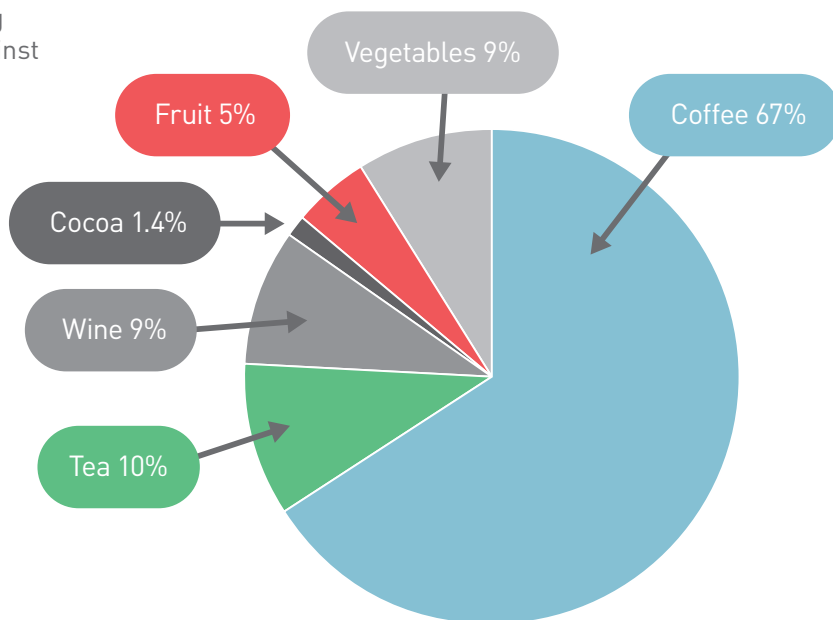


Figure 4: Dietary analysis of polyphenol consumption in a French population

Other coffee components

Research has suggested that a further compound present in coffee, quercetin,

could have a key role in preventing neurotoxicity of key cells. The researchers found

that quercetin, along with flavones, chlorogenic acid and caffeine, could protect

SH-SY5Y cells from neurotoxins, in turn having a positive impact on the incidence

of Alzheimer's Disease. However, further work is required to confirm this³⁴.



Conclusion

Alzheimer's Disease is a multifactorial disease with a vast array of risk factors from genetic to lifestyle. An emerging body of research suggests that nutrition can play an important role in reducing the risk of Alzheimer's. Epidemiological studies have suggested that there may be an association between moderate coffee consumption and a reduced risk of developed Alzheimer's, however further research is required to fully understand the nature of this relationship.

The literature suggests three ways to derive optimum benefit from coffee consumption:

- **Timing** – it should begin early, before the onset of symptoms of dementia.
- **Duration** – it should be regular and lifelong.
- **Amount** – it should be moderate, at 3-5 cups of coffee per day.





The annual **Alzheimer Europe conference** is a forum that brings together a range of delegates including; academics and researchers, health care professionals, policy makers and civil servants, industry representatives, carers and people with dementia.

At the 24th annual conference on 23rd October 2014, ISIC hosted a symposium on nutrition, coffee and cognitive decline, with an expert panel from across Europe:

- **Iva Holmerova** - vice chairperson, Alzheimer Europe (Chair)
- **Neville Vassallo** - senior lecturer in physiology and biochemistry, University of Malta
- **Arfan Ikram** - assistant professor in neuroepidemiology, Erasmus Medical Centre Rotterdam
- **Astrid Nehlig** - research director, French Medical Research Institute (INSERM), Strasbourg.

This third edition of the report was updated in September 2016 to include the latest research in this area.

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 has also supported 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 respects scientific research ethics in all its activities. ISIC's communications are based on sound science and rely on evidence and 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.

www.coffeeandhealth.org



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