

Dietary Flavonoid Intakes Impact Self-Assessment of Cognitive Decline

This decades-long prospective study of over 77,000 health professionals is among the first to demonstrate that a higher intake of flavonoids is associated with significantly reduced risk for subjective cognitive decline (SCD). Especially strong protection was found for flavones, flavanones, and anthocyanins, though other flavonoid subclasses were also associated with reduced SCD risk.

The global human population is collectively aging, to an unprecedented extent. This rise in the average age of humans is accompanied by increases in the prevalence of and social burden related to cognitive impairment. Dietary flavonoids have demonstrated considerable neuroprotective qualities in research, yet past epidemiologic studies examining the effects of flavonoid consumption on the development of dementia and other cognitive conditions have shown inconsistent results.

Part of this challenge lies in the fact that dementia typically has a lengthy preclinical phase—often twenty years or more—during which individuals may subjectively be aware of subtle alterations in their own cognitive function before the appearance of overt clinical change. Subjective cognitive decline (SCD) has been found to relate strongly to objective cognitive changes as well as subsequent cognitive decline. For these reasons, assessing dietary flavonoid intakes through the decades prior to clinically observable modification of cognitive function may present a more meaningful approach to investigating their later-life effects.

This prospective study is one of the largest and longest to examine flavonoid intakes and cognitive health, and involved 49,493 female registered nurses (aged 30-55 years at baseline) from the Nurses Health Study (NHS) as well as 27,842 male health professionals from (aged 40-75 years at outset) from the Health Professionals Follow-Up Study (HPFS). NHS participants



were followed from 1984 to 2014; HPFS participants from 1986 to 2012. Dietary information was collected from study subjects according to validated procedures each two to four years for over 20 years. SCD was assessed by validated questionnaires twice in the final two to four years of the investigation, when participants' mean ages were 76.3 years among females and 73 years among males. Dietary data on flavonoid intakes were derived from federal database values, and focused on six subtypes of flavonoids:

- Flavones (such as luteolin and apigenin)
- Flavanones (like hesperetin and naringenin)
- Anthocyanins (delphinidin, pelargonin, etc.)
- Flavonols (like quercetin and kaempferol)
- Flavan-3-ol monomers (catechins, epicatechins, etc.)
- Flavonoid polymers (such as proanthocyanidins and tannins)

Study subjects were classed into age-controlled quintiles of consumption level for total flavonoids as well as the flavonoid subtypes. Results were controlled for age, body mass index, physical activity level, and numerous other relevant health, dietary, and lifestyle factors.

Cognitive dysfunction is an increasingly prevalent age-related condition for which few reliable methods of prevention or intervention are known.

According to findings from this epidemiologic study, earlier, greater, and longer-term consumption of total flavonoids and of flavones, flavanones, and anthocyanins may confer significant benefits upon later-life cognitive function.

Clinical Highlights

Major findings from data gathered over almost 30 years of observation of 77,335 health professionals' habitual intakes of flavonoid-containing foods and later development of subjective cognitive decline (SCD) include the following:

- Intakes of every flavonoid subtype demonstrated an inverse relationship to SCD risk.
- Overall, the strongest protective associations were found for flavones, flavanones, and anthocyanins. Subjects in the highest quintiles of consumption of these flavonoids showed 38%, 36%, and 24% lower risk for SCD, respectively, compared to those at the lowest intake levels. Researchers estimated that the 38% risk reduction was comparable to being 3-4 years younger than actual chronological age.
- Strongest dose-dependency relationships between flavonoid subtypes and SCD protection were observed for flavones and anthocyanins.
- Lower flavanone intakes were found to independently predict future SCD.
- A mean total flavonoid intake of 345 mg per day was found among study subjects in the highest quintile of overall flavonoid consumption, and those with higher total flavonoid



intakes showed consistently greater intakes of all flavonoid subtypes. Highest intakes by flavonoid subtype were for flavonoid polymers, while lowest intakes by subtype were for flavones.

- Specific flavonoid-rich foods associated with SCD protection included, in descending order, brussels sprouts, strawberries, cauliflower, spinach, yams/sweet potatoes, blueberries, yellow/orange winter squash, cooked carrots, peaches/apricots/plums, cantaloupe, tomato sauce/juice, applesauce, peppers, broccoli, cabbage, lettuce, raw tomatoes, and grapefruit.
- Top foods contributing to flavone intakes included orange juice, oranges, peppers, celery, and red wine.
- Top foods contributing to flavanone intakes included orange juice, oranges, grapefruits, and grapefruit juice.
- Top foods contributing to anthocyanin intakes included blueberries, strawberries, apples, and red wine.
- Higher intakes of flavones, flavanones, strawberries, orange juice, and brussels sprouts were associated with SCD protection at every follow-up time point during the study.
- Among NHS study subjects, greater consumption of total flavonoids, berries, and anthocyanidins was previously found to be associated with less cognitive decline later in life.
- Study subjects who were non-smokers or had higher carotenoid phytonutrient intakes were found to have greater consumption of flavonoids.

The researchers noted a strong positive relationship between SCD scores and cardiovascular disease, heavy smoking, APOE E4 genotype (strongly linked to lipid dysregulation and vascular disease), hypertension, elevated cholesterol, depression, and type 2 diabetes. These observations lend validity to the study's other findings.

A particularly interesting finding from the study was that SCD protection associated with higher intakes of flavones and flavanones was heightened by 5-6% for every decade of decreasing age at time of consumption; in effect, earlier habitual consumption of these flavonoids augmented SCD protection in a time-dependent fashion.

NUTRITION CONCLUSION

Subjective cognitive decline has previously been linked to the incidence of clinical cognitive disorders. Results from this comprehensive and well-designed study suggest that regular, generous consumption of flavonoid-rich foods (like berries, cruciferous vegetables, and citrus fruits) is associated with better subjective cognitive function later in life.

