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Updates in Neurology: The Neuroprotective Role of Dietary Polyphenols

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Polyphenols are a group of naturally occurring bioactive compounds found in high amounts in many fruits, vegetables, seeds, nuts, herbs, and spices. It's been known for a while that polyphenols are important antioxidants. For example, the dopamine-preserving effect of catechin-rich polyphenol extracts from green tea observed in animal models of Parkinson's disease, is thought to be due in part to the ability of polyphenols to modulate the antioxidant activity of superoxide dismutase.[1] Now, an increasing number of studies suggest that dietary polyphenols have potent anti-inflammatory and neuroprotective properties as well. In particular, studies report that polyphenols protect neurons from neurotoxins; modulate neuroinflammation; and improve memory, learning, and cognitive function. The traditional Mediterranean diet is very rich in polyphenol-containing plant foods, which is one reason it's thought to offer protection against neurodegeneration and cognitive decline.

Dietary Polyphenols and Neuroprotection

Neuroinflammation is a common feature of neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and Multiple Sclerosis. Persistent oxidative stress is known to play a significant role in the neurodegenerative process (as well as in the aging process in general). It makes sense, then, that polyphenols could have neuroprotective effects in their capacity as powerful antioxidants, but it turns out in addition to being free-radical scavengers, they influence a variety of molecular mechanisms including gene expression. In vitro and animal studies show that polyphenols are able to:[2]

- Decrease neuroinflammation
- Protect against beta-amyloid plaque formation
- Protect against neuronal damage from glutamate toxicity
- Promote synaptic plasticity and nerve growth

Human studies have also shown benefits, including improving cognitive performance.[3]

In fact, benefits observed in human studies have been attained from using amounts of polyphenols akin to levels that would be available from the diet.[4]

Polyphenols and Microglial Cells

Neuroinflammation is a critical aspect of the brain's defense mechanisms, but when it's excessive or unresolved it contributes to the underlying neuronal loss and damage characteristic of neurodegenerative disorders. Neuroinflammation activates microglial cells, which are a foremost component of the brain's innate immune response. Recent studies have highlighted an intriguing property of activated microglial cells: they can be induced into two different forms or phenotypes depending on the predominant needs of the CNS environment in which they find themselves. This means they can shift into having either pro-inflammatory/neurotoxic or anti-inflammatory/neuroprotective effects. Amazingly, dietary polyphenols are able to influence microglial cells to shift in the direction of being the resolving rather than the activated phenotype. As a result, microglial cells will produce anti-inflammatory cytokines and contribute to neuroregeneration.[5]

Types of Polyphenols

Polyphenols comprise an enormous set of plant compounds. Over 8000 types have been identified so far. For simplicity, polyphenols can be divided into two major categories: flavonoids and nonflavonoids.

Flavonoids

Over 4000 distinct flavonoids are known at this point, and they account for 50 to 60% of all polyphenol compounds. Some well-known flavonoids include luteolin, quercetin, genistein, hesperetin, and catechins (often referred to as proanthocyanidins).

Nonflavonoids

This group includes resveratrol, which is found in grapes and wine; stilbenes and lignans, found in fruits, vegetables, seeds, and whole grains; capsaicinoids found in chili peppers; and curcumin found in turmeric.[6]

Dietary Sources of Polyphenols

Culinary and medicinal plants and spices are great dietary sources of polyphenols.

In a study that identified the 100 foods richest in polyphenols, cloves came out on top.

Other dietary sources all of which were high up on this list include cocoa powder, blueberries, blackberries, strawberries, red raspberries, black currants, plums, sweet cherries, apples, pomegranate juice, black beans, white beans, chocolate, green tea, and black tea.[7]

Let's focus now on some specific dietary polyphenols.

Isoflavones

Isoflavones are mostly found in the leguminous family of plants. Dietary sources high in isoflavones include beans (particularly soybeans), chickpeas, pistachios, split peas, lima beans, fava beans, lentils, green tea, and flaxseeds.[8]

Nuts

Many nuts, including hazelnuts, almonds, pecans, and walnuts are excellent sources of polyphenols.[9,10]

Nettles (*Urtica dioica*)

The aerial parts of the nettle plant are rich sources of polyphenols. In an animal study, nettle supplements and regular swimming exercise were shown to improve the adverse effect of brain injury. The analysis showed that nettle supplementation had an antioxidant effect, and also down-regulated inflammatory transcription factors, as well as promoting learning.[11]

Quercetin

Quercetin has been shown to improve memory, learning, and cognitive functions in several in vitro and animal models.[12]

Rosmarinic Acid

Rosmarinic acid is a polyphenol compound present in plants such as rosemary, sage, lemon balm, mint, and sweet basil. A growing body of research suggests that rosmarinic acid may be protective against neuronal cell death and beta-amyloid plaque formation.[13]

Curcumin

Curcumin is a polyphenol compound found in turmeric (*Curcuma longa*), that has been studied extensively for its systemic anti-inflammatory properties. Curcumin also appears to prevent the amyloid plaque deposition associated with neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and Huntington's disease. In addition, it decreases neuroinflammation through a variety of mechanisms including inhibiting proliferation of microglial cells, and reducing levels of inflammatory cytokines such as tumor necrosis factor (TNF), interleukin-1 (IL-1), and interleukin-6 (IL-6).[14]

Curcumin is more lipophilic than hydrophilic, which allows it to be absorbed through the blood-brain barrier. It is better absorbed when eaten with fat, and can be detected in the cerebrospinal fluid.[15] Curcumin and turmerone are the major bioactive compounds of *Curcuma longa*. Although tumerone is not technically a polyphenol, it may promote the production of neural stem cells thereby enhancing neuron generation and repair.[16]

Resveratrol

Resveratrol is a polyphenol found in highest concentrations in the skin and seeds of berries and grapes, and consequently, in red wine (and to a lesser extent in rose and white wine).

Rich sources of polyphenols include herbs, spices, berries, tea, cocoa, dark chocolate, ground flaxseeds, chestnuts, pecans, almonds (with skin), and many other plant foods. A number of different types of berries are rich in polyphenols, including blueberries, blackberries, strawberries, and raspberries. Resveratrol has been shown to inhibit the formation of beta-amyloid plaque,[17] and to promote remyelination in an animal model of MS.[18]

Bioavailability of Dietary Polyphenols

The physiological activity of polyphenols is influenced by several factors including the health of a person's metabolism, intestinal absorption, and the bioavailability of the polyphenol itself. Gut bacteria ferment polyphenols to produce short-chain fatty acids, which themselves have neuromodulatory effects. It also appears that polyphenols can cross the blood-brain-barrier, and as a result, may have direct neuroprotective and neuromodulatory effects within local brain tissue. There is certainly enough growing evidence of their protective effects for you to advise your patients with neuroinflammatory and neurodegenerative conditions to

incorporate foods and beverages high in polyphenols into their health and wellness lifestyle choices.[19]

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