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Editorial

Food for Thought: The Impact of Polyphenols on Brain Health

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Dementia and associated cognitive decline, as well as age-related neurodegenerative diseases, lead to a drastic reduction in quality of life in later years and are some of the greatest and most urgent public health issues facing Western societies today. Despite the projected increase in age-associated dementia (three-fold by 2060), there is lack of effective disease-modifying treatments and no established lifestyle guidelines for preventing and/or delaying dementia [1]. Yet, modifiable risk factors (e.g. such as diet, physical fitness), can account for as much as 35% of the dementia burden later in life [2].

Polyphenols are secondary metabolites produced in plants that are important for their growth and protection. Present in most fruits and vegetables, polyphenols have for more than 25 years attracted researchers looking into the beneficial effects of consumption of polyphenol-rich foods for human health, and particularly brain health. Epidemiological evidence has clearly indicated that diets rich in polyphenol-rich foods (e.g. Mediterranean diet) can slow age-related cognitive decline and even reduce the risk of dementia [3, 4].

This Special Issue of Brain Plasticity includes 1 Research Report and 3 in-depth review articles that together address the evidence for benefits of polyphenol intake on human cognitive function, whilst also providing valuable insight into mechanisms of action in the context of neurological disorders (e.g. Alzheimer's Disease), as well as highlighting vital questions in the field, such as polyphenol accessibility to the central nervous system.

The Special Issue begins with an article critically evaluating the evidence (present in systematic reviews and meta-analysis) for the impact of polyphenol intake and cognitive function in humans. The authors identify important limitations in the literature in regards to methodological heterogeneity which leaves key questions unanswered, particularly in regards to the identification of effective doses, intervention duration or populations most likely to benefit. The authors also attempt to identify areas of cognitive function that are more likely to be improved by polyphenol interventions, further highlighting the importance of standardizing what is considered a 'cognitive benefit' across studies. Areas for improvement in future human research in this area are clearly outlined and are vital to strengthen the reliability of the evidence base of polyphenol intake in cognitive function [5].

The following literature review article provides a comprehensive account of the evidence of the flavonol fisetin on preventing the development and progression of neurological disorders. More specifically, it focus on pre-clinical studies that investigated the beneficial effects of fisetin in models of Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, ischemic stroke, hemorrhagic stroke and traumatic brain injury. Human intervention trials are only now starting to emerge, with encouraging improvements in therapeutic outcomes coming from a study using fisetin

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as an adjuvant therapy for ischemic stroke. Finally, authors further elaborate and discuss several novel mechanisms of action [6].

The third article provides a detailed analysis of the evidence for developing specific flavonoids as therapeutics for Alzheimer's Disease (AD), presenting a comprehensive insight into underlying mechanisms of action focused on regulation of tau pathology, one of the key features of the disease. Most importantly, the authors make a strong case for considering how metabolism and bioavailability of flavonoids *in vivo* may impact the use of flavonoids as therapeutic agents in AD. In that regard, the authors clearly identify key strategies to successfully incorporate metabolism and bioavailability in pre-clinical research and make it more translatable to humans [7].

Finally, the last article of this Special Issue tackles a critical question regarding bioavailability of polyphenol metabolites in brain tissue. The ability of polyphenols to directly affect the brain may in part depend on their ability to cross the blood-brain barrier (BBB) and enter the central nervous system. Despite, considerable research on the potential neuroprotectant potential of polyphenols, the question of which polyphenol metabolites reach the brain remains an 'underexplored journey', as the authors describe. In this important article, the authors critically evaluate *in silico*, *in vitro* and *in vivo* studies exploring the potential mechanisms of transport of polyphenol metabolites through the BBB [8].

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