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Natural mood foods: The actions of polyphenols against psychiatric and cognitive disorders

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Abstract

Objectives—Polyphenols, natural compounds found in plant-based foods, possess special properties that can battle oxidative stress and stimulate the activation of molecules that aid in synaptic plasticity, a process that underlies cognitive function. Unlike many traditional treatments, polyphenols affect a broad range of mechanisms in the brain that can assist in the maintenance of cognitive and mental health, as well as the recovery from neurodegenerative diseases. Examining the molecular basis underlying the link between food intake and brain function has presented the exciting possibility of using diet as a viable method to battle cognitive and psychiatric disorders.

Methods—We will discuss the molecular systems that link polyphenols, the gut, and the brain, as well as introduce published human and animal studies demonstrating the effects of polyphenol consumption on brain plasticity and cognition.

Results—By influencing cellular energy metabolism and modulating the signaling pathways of molecules involved with brain plasticity, dietary factors – formerly recognized for just their effects on bodily systems – have emerged as affecters of the brain.

Conclusion—Thus, the consumption of diets enriched with polyphenols may present the potential of dietary manipulation as a non-invasive, natural, and inexpensive therapeutic means to support a healthy brain.

Keywords

BDNF; Cognition; Metabolism; Polyphenol; Psychiatric disorder; Synaptic plasticity

Introduction

As the prevalence of neurodegenerative and psychiatric disorders steadily increases, cost-effective and functional methods of treatment are reaching an unforeseen demand. While it is true that extensive research has been conducted in the biological field of brain-specific diseases, only recently has considerable effort been dedicated to study the influence of lifestyle factors like diet and exercise habits on brain health. Emerging research demonstrates that dietary and exercise factors can affect the maintenance and development of neurons and protect the brain from insult associated with neurological illnesses or injuries. This link between brain health and lifestyle factors has spurred researchers to explore the use of nutrition as possible therapeutic means to enhance neurological function

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and cognition. Nutrients that have been recognized in the past solely for their beneficial effects on the body are now known to possess protective properties against brain-specific disorders. In particular, polyphenols – chemical compounds abundant in plant-derived foods such as fruits and vegetables – have garnered special attention for their broad spectrum of molecular and cellular actions against neurological degeneration. For example, the polyphenols epigallocatechin gallate (EGCG), found in green tea, and curcumin, found in the turmeric plant, have been strongly associated with higher cognitive function, better mood, and protective effects against various brain diseases. As evidence demonstrating the neuroprotective features of polyphenols grows quickly, the exciting possibility of dietary regulation as a therapeutic tactic for brain maintenance and protection is becoming more and more likely.

In this review, we will discuss the impact of polyphenols on brain function, neurodegenerative disorders, and psychiatric disorders. We first delve into the molecular basis of how foods abundant in polyphenols influence mental health and cognition, namely via energy metabolism and modification of signaling pathways and gene expression involved in synaptic plasticity, or the ability of a neuron to strengthen and change synaptic connections. Energy metabolism, the chemical process through which living organisms break down foodstuffs to usable energy sources, was formerly recognized solely as a source of energy provision, but is now known to modulate cellular processes that affect synaptic plasticity and brain health. Additionally, we will be discussing molecular and chemical specifics of polyphenolic action on the brain, followed by a special focus on two of the most studied polyphenols: curcumin and EGCG.

The link between food and cognition

Energy metabolism and brain function

Food consumption and physical activity stimulate metabolic processes present in mitochondria, the main vessels of energy metabolism in the body that break down organic matter into usable energy. Mitochondrial activity may modulate signaling pathways and molecules that are linked to neuronal function. This relationship between metabolic activity and neuronal function indicates that our dietary and exercise habits can influence the molecular mechanisms that define our mental capacity to learn. Indeed, it is not surprising that energy metabolism is so closely affiliated with the maintenance of brain function, as the brain is the largest consumer of energy in the body, utilizing more than 20% of all the oxygen consumed during mitochondrial respiration.[1] The effect of energy metabolism on brain health is mediated through molecules like brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1, molecules that influence both energy balance and neuronal plasticity (Fig. 1). Most active in regions of the brain associated with cognition –namely, the hippocampus and cerebral cortex –BDNF is a neurotrophin known for its influence on the maintenance, survival, growth, and differentiation of neurons. Crucial for normal neural development, BDNF stimulates synaptic plasticity in neurons, enhancing learning capacity and memory formation.[2] In fact, BDNF is so essential in the brain's cognitive processes that deletion of the BDNF gene was found to weaken memory retention and inhibit long-term potentiation, a cellular mechanism underlying memory, in rats.[3] It was also demonstrated that BDNF affects various aspects of energy metabolism and a mutation in BDNF receptor tyrosine kinase can lead to tips of the brain's energy balance, leading to metabolic disorders such as obesity.[4] Moreover, the intracerebroventricular administration of BDNF in rats was shown to decrease energy intake and body weight, and enhance insulin receptor signaling in the liver of diabetic mice.[5,6] These studies reveal the close involvement of BDNF in the processes of both energy metabolism and neuronal plasticity, demonstrating the link between dietary intake and brain function.

Metabolic dysfunction can harm the brain

Unfortunately, extreme metabolic activity due to high caloric intake can lead to the excessive production of brain-harmful oxidative by-products called reactive oxygen species (ROS). ROS are oxygen-containing molecules that are classified as either radicals (having unpaired valence shell electrons) or non-radicals, and are known to be highly reactive, readily oxidizing stable molecules. In aerobic organisms, production of ROS is a normal event following the use of molecular oxygen in oxidative phosphorylation during mitochondrial metabolism. However, while moderate production of these oxidative species is expected, the excessive production of ROS can pose serious neurological injury, oxidizing and damaging biological targets such as DNA, lipids, and proteins, and altering key cellular response systems and pathways (Fig. 1). Because the brain must consume a large amount of molecular oxygen to function properly, the likelihood of damaged biomolecule accumulation caused by ROS is high, especially with aging.[7] Fortunately, the brain also naturally produces endogenous antioxidant defense enzymes that act as free radical scavengers, counteracting oxidative stress caused by ROS. Antioxidant defense enzymes such as superoxide dismutase, glutathione peroxidase, and catalase aid in the maintenance of metabolic homeostasis and protect crucial neuronal components from harmful oxidation. Although the presence of these antioxidants is normally sufficient to defend the brain from oxidative insult, it can be overwhelmed during periods of unwarranted oxidative production, such as during excessive consumption of calories.[8] Thus, a proper balance between oxidants and antioxidants is needed to avoid the repercussions of oxidative damage. Accordingly, choosing the right foods – such as a diet high in antioxidant-rich polyphenols – is crucial in order to reap the neurological benefits they offer.

Fighting the blues: Polyphenols and the battle against cognitive and mental illnesses

Up to one billion people around the world are affected by neurological diseases such as Alzheimer’s disease and Parkinson’s disease. In a lifetime, one in four people are prone to mental disorders, including depression, bipolar disorder, and schizophrenia. The likelihood of these neurodegenerative diseases has been closely associated with neuronal dysfunction and low levels of molecules essential in daily brain function, such as the aforementioned BDNF.[8] The varying levels of BDNF in healthy patients and patients with brain disorders implicate the potential therapeutic role of BDNF in the treatment of such disorders. Furthermore, as noted earlier, the imbalance between the production of ROS and antioxidants results in oxidative stress, which has also been associated with many neurological and psychiatric diseases. Unfortunately, with the growing prevalence of psychiatric disorders in the world, more and more anti-depressant therapies are being developed, but few have proved to be successful. Thirty percent of patients fail to respond to current drug therapies and 70% do not achieve complete remission.[9] Thus, as patients become disenchanted with the risks and unwarranted side effects of drug therapies, natural alternatives are emerging as potential solutions to alleviate depressive symptoms. For example, Foods high in dietary polyphenols, found in colorful fruits, vegetables, spices, teas, and wines, are becoming popular with their powerful antioxidant and anti-inflammatory activities in the brain. Polyphenols with notable radical-scavenging activity include curcumin from turmeric and EGCG from green tea. In addition to their antioxidant and anti-inflammatory activity, polyphenols have been coupled with the increased expression of BDNF, assisting in the reversal of neuronal atrophy and behavior deficits.[10] Here, we discuss the specific actions of dietary polyphenols in maintaining brain health and battling brain-related disorders.

The molecular mechanisms of polyphenols against psychiatric and cognitive disorders

Polyphenols are natural organic compounds produced by plants as defense mechanisms against pathogen attacks, ultraviolet radiation, and physical damage. Giving plant-derived foods and beverages their characteristic bitter taste, over 8000 polyphenolic compounds of plant origin have been identified, many of which are widely studied and recognized for their brain-protective properties.[11] Considerable attention has been ascribed to botanical and herbal polyphenols found in foods and dietary supplements, as they are relatively inexpensive, have fewer perceived side effects than many pharmaceuticals, and are non-invasive compared to other forms of treatment. Polyphenols are comprised of multiple phenolic groups and may associate with various carbohydrates and organic acids. Chemically, they can be separated into 10 different groups based upon the number of phenol rings they contain and the substances attached to the rings. With a distinctive 2-phenyl-1,4-benzopyrone structure, flavonoids comprise the most abundant polyphenolic group and include the subgroups anthocyanins, isoflavanoids, flavanols, flavanones, flavones, and flavanols (Fig. 2). Upon consumption, polyphenols are available in the form of esters, glycosides, or polymers that cannot be absorbed in the gut. They are hydrolyzed by intestinal enzymes and conjugated via methylation, sulfation, and glucuronidation, after which they can be absorbed by the gut and travel to various bodily tissues and organs such as the brain.[12] However, due to the diverse susceptibilities of phenolic compounds by gut enzyme metabolism, their bioavailability can vary from very low to very high.[10] A polyphenol's bioavailability is also determined by its ability to cross the blood–brain barrier (BBB), a separation between blood and brain extracellular fluid that manages the influx of various metabolites, nutrients, and drugs. Many polyphenols have been claimed to possess neuroprotective effects, but a number of polyphenols has been demonstrated to be incapable of crossing the BBB, meaning they exhibit poor bioavailability or affect their health benefits in the brain via other pathways (Table 1).[13]

Polyphenols act as antioxidants through the donation of a hydrogen atom from their hydroxyl groups, resulting in the creation of a phenoxyl radical that can either undergo the release of another hydrogen or a reaction with another radical to create a stable compound.[1] In other words, the polyphenol, X-OH, reacts with the ROS, R, by giving it a hydrogen atom through homolytic rupture of the hydroxyl bond. The products of this reaction are stabilized oxygen species, R-H, and phenoxyl radicals that can be stabilized by reactions with other radicals. As well as giving plants their color pigmentation, conjugated double bonds found in phenol groups are capable of stabilizing free radicals through delocalization of unpaired electrons.[14,15] In addition to their antioxidant properties, research has shown that polyphenols can exert their neuroprotective properties through modulation of specific cellular signaling pathways involved with cognitive processes such as synaptic plasticity – notably, pathways that signal cAMP-response element-binding protein (CREB), a transcription factor linked with genes that express BDNF. The importance of CREB in brain function is emphasized by studies that demonstrate impairments in memory formation induced by the disruption of CREB activity and similarly, accelerations in memory formation stimulated by increased CREB activity. Polyphenols can directly modulate these signaling pathways and induce CREB, and subsequently BDNF, activation.[16]

Studies demonstrating polyphenolic action on the brain

Recent studies have identified several polyphenols that can affect neuronal and synaptic processes. While many of these studies were performed *in vitro*, it must be noted that the actions of polyphenols may differ and entail more complicated actions *in vivo*. Polyphenols of the flavonoid group comprise a majority of the studies on the neuroprotective role of phenolic compounds. Studies on rats demonstrate that polyphenols can boost cognitive processes by modulation of extracellular signal-regulated kinase (ERK)/CREB signaling

pathways and protection from ROS-specific damage such as lipid peroxidation and neuroinflammation.[17] The ERK pathway is usually affiliated with pro-neurotrophin signaling through stimulation of CREB. Resveratrol, a phenolic compound abundant in berries, grapes, red wine, and peanuts, has been found to protect neurons against Abeta-induced toxicity and attenuate degeneration of memory and Abeta pathology in rats.[1] These animal studies suggest that the powerful neuroprotective effects of polyphenols are mediated through a variety of methods that range from protection against oxidative stress to interaction with signaling pathways involved in maintaining energy homeostasis. Chlorogenic acid, a phenolic compound abundant in plums, apples, and cherries, induced a decrease in anxiety-like behaviors in mice, measured by the light/dark test, the elevated plus maze, and the free exploratory test.[18] This reduction in anxious disposition derived from the combination of chlorogenic's anxiolytic and antioxidant properties. In a rat model of depression induced by exogenous corticosterone administration, it was discovered that curcumin treatment significantly suppressed depression-like behavior and slowed down the deterioration of brain BDNF levels. Depression levels were measured by the percentage of sucrose consumption and the forced swim test, while measurement of BDNF levels was narrowed to the hippocampus and frontal cortex of rats.[19] Several studies also suggest that the antidepressant activity of curcumin involves interaction with monoamine oxidase (MAO), an enzyme essential in the catabolism of monoamines and the inactivation of monoaminergic neurotransmitters such as serotonin, dopamine, and norepinephrine. A long-debated hypothesis known as the 'monoamine hypothesis' speculates that the physiological foundation of depression derives from deficient levels of monoamine neurotransmitters such as those listed earlier.[20] Accordingly, a study involving mice found that the coadministration of curcumin along with piperine, an alkaloid present in black pepper, inhibited the action of MAO enzymes, thus inhibiting the breakdown of monoaminergic neurotransmitters, and increasing serotonin and dopamine levels.[21]

Human studies display similar effects as animal studies. For example, a study found improved cognitive function in elderly Asian subjects who frequently consumed curry compared to those who rarely consumed curry.[14] In fact, the wide use of turmeric in India is believed by some to contribute to the low incidence of Alzheimer's disease in the country. A similar study discovered that those who frequently drank green tea in comparison with those who rarely drank green tea were less likely to experience cognitive impairment, possibly explaining the low prevalence of cognitive disorders in Japan.[22] This cross-sectional study was conducted in Sendai, Japan, in which the green tea consumption of over 1000 elderly Japanese individuals was assessed in juxtaposition with self-noted levels of depression. Green tea consumption over a period of 1 month was evaluated using a self-administered questionnaire while depressive systems were measured with a 30-item geriatric depression scale ranging from 11 (mild and severe depression) to 14 (severe depression). According to results, higher green tea consumption closely affiliated with a lower prevalence of depressive symptoms, indicating the potential therapeutic effects of green tea on depression. Likelihood for mild and severe depressive symptoms when green tea consumption was ≤1 cup/day was compared to the likelihood when green tea consumption was 2–3 cups/day and ≥4 cups/day. After adjustments for other factors influencing depressive symptoms, such as drinking habits, history of cardiovascular disease, and diabetes, the study found that the scores for mild and severe depressive symptoms were 1.00 – a reference value –for ≤1 cup/day, 0.96 for 2–3 cups/day, and 0.56 for ≥4 cups/day. In other words, those who drank ≥4 cups/day experienced a 44% lower prevalence of depressive symptoms than those who drank ≤1 cup/day. Although the results of this study require scientific examination for validation, they are in general agreement with various animal studies demonstrating the neuroprotective effects of polyphenols.[23]

Here, we focus on the defensive actions of two major polyphenols – curcumin and EGCG – against common neurological and mental disorders.

Curcumin

Curcumin is the primary pharmacological agent and supplier of yellow pigmentation in the turmeric plant, a culinary and medicinal ingredient utilized regularly in many types of curries. In addition to antioxidant and anti-inflammatory activities, curcumin possesses antiamyloidogenic, anticarcinogenic, antiviral, and antifungal properties that have been recognized and used since 1900 BC to treat various illnesses.[24] Evidence shows that curcumin can alleviate symptoms of depression by enhancing neurogenesis in the hippocampus and frontal cortex of the brain.[9] In a recent study, rats were subjected to a chronic stress protocol for 20 days, resulting in performance impairments in the shuttle-box task and numerous physiological setbacks, such as a reduction in BDNF and ratio of pCREB to CREB in hippocampal and frontal cortical regions of the brain. Chronic curcumin administration reversed these stress-induced changes, altering neurotrophin levels in a manner comparable to the tricyclic antidepressant imipramine.[25] Curcumin not only boosts neuronal function, but it can also protect against the effects of neuronal degeneration. A recent study induced oxidative stress in rats via traumatic brain injury, which was marked by increased carbonyl levels – implicative of protein oxidation involved with free radical formation. Treatment with curcumin in the diet decreased carbonyl levels post-injury, demonstrating its antioxidant properties. Wu A, Ying Z, Schubert D, Gomez-Pinilla F. Brain and spinal cord interaction: a dietary curcumin derivative counteracts locomotor and cognitive deficits after brain trauma. Neurorehabil Neural Repair 2011;25:332-42. Additionally, in a similar study, rats were subjected to a mild fluid percussion injury in which curcumin supplementation counteracted cognitive impairment by increasing levels of BDNF, CREB, and synapsin I, a protein that influences synaptic events.[26] Moreover, due to its lipophilicity, curcumin can easily cross the BBB and directly induce neuroprotection.

Epigallocatechin gallate

Abundant in green tea, EGCG is a natural catechin polyphenol that has been utilized in China as medicine for at least 4000 years. Now available in botanical supplement form, EGCG is most renowned for its high antioxidant activity and its ability to alleviate symptoms of stress and depression. A recent study supplemented psychological stress rats with green tea polyphenols and measured the changes in antioxidative capacity in brain tissue and cognitive performance as assessed by behavioral tests. Alterations in ROS and malondialdehyde, a highly reactive product of oxidized polyunsaturated lipids, were significantly different from those of the control group such that experimental rats displayed fewer signs of stress. Cognitive performance, impaired by psychological stress, was improved by green tea polyphenol supplementation.[27] In another study, long-term administration of green tea polyphenols modified CREB signaling cascade by increasing levels of hippocampal CREB phosphorylation and BDNF, and prevented age-related memory decline of aged female mice.[28,29] Similar to the study in Japan, a study with 716 community-living Chinese adults aged 55 or higher examined the relationship between tea consumption habits and cognitive function. Frequency of tea consumption was self-reported and cognitive function was assessed by a series of neuropsychological exams focusing on attention, memory, and information processing, and was scored by the Mini-Mental State Examination. It was found that tea consumption correlated with better cognitive performance in Chinese older adults.[30]

Conclusion

As molecular evidence implicating the link between food intake and brain utility quickly grows, implementing diet and exercise as therapeutic means to fortify neuronal function and battle neurodegenerative disorders could provide a practical alternative to standard treatment. Polyphenols especially pose a positive effect on the brain by modulating synaptic transmission and enhancing cognitive function with their antioxidant properties, engaging signaling pathways that link molecules that act at the interface between cellular metabolism and synaptic plasticity. No longer is feeding exclusively associated with bodily functions; it is quickly gaining recognition for its bearings on brain function and consequently, cognition, mood, and associated illnesses. Moreover, recent research indicates that other lifestyle factors such as exercise and sleep can supplement a healthy diet's effects on mental health.[8] This has strong implications for public health and can render healthy brain function an attainable goal for everyone simply by practicing healthy everyday habits – for example, pursuing a diet high in polyphenols. Yet, while evidence portraying the positive effects of polyphenols is abundant, more research is needed before they can be regarded as self-sufficient treatments. Future research directions include the stability of neuronal changes induced by polyphenol consumption and the dosage and frequency of consumption needed for significant results. Regardless, the effects of diet on brain function is undeniable, and supplemented with other healthy lifestyle choices, have major implications for the battle against neurological and psychiatric disorders.

Acknowledgments

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References

1. Rossi L, Mazzitelli S, Arciello M, Capo CR, Rotilio G. Benefits from dietary polyphenols for brain aging and Alzheimer's disease. Neurochem Res. 2008; 33:2390–400. [PubMed: 18415677]
2. Zuccato C, Cattaneo E. Brain-derived neurotrophic factor in neurodegenerative diseases. Nat Rev Neurol. 2009; 5:311–22. [PubMed: 19498435]
3. Ma YL, Wang HL, Wu HC, Wei CL, Lee EH. Brain-derived neurotrophic factor antisense oligonucleotide impairs memory retention and inhibits long-term potentiation in rats. Neuroscience. 1998; 82:957–67. [PubMed: 9466420]
4. Yeo GS, Connie Hung CC, Rochford J, Keogh J, Gray J, Sivaramakrishnan S, O'Rahilly S, Farooqi IS. A de novo mutation affecting human TrkB associated with severe obesity and developmental delay. Nat Neurosci. 2004; 7:1187–9. [PubMed: 15494731]
5. Pelleymounter MA, Cullen MJ, Wellman CL. Characteristics of BDNF-induced weight loss. Exp Neurol. 1995; 131:229–38. [PubMed: 7534721]
6. Tsuchida A, Nakagawa T, Itakura Y, Ichihara J, Ogawa W, Kasuga M, Taiji M, Noguchi H. The effects of brain-derived neurotrophic factor on insulin signal transduction in the liver of diabetic mice. Diabetologia. 2001; 44:555–66. [PubMed: 11380073]
7. Halliwell B. Oxidative stress and neurodegeneration: where are we now? J Neurochem. 2006; 97:1634–58. [PubMed: 16805774]
8. Gomez-Pinilla F. Brain foods: the effects of nutrients on brain function. Nat Rev Neurosci. 2008; 9:568–78. [PubMed: 18568016]
9. Kulkarni S, Dhir A, Akula KK. Potentials of curcumin as an antidepressant. Sci World J. 2009; 9:1233–41.
10. Wollen KA. Alzheimer's disease: the pros and cons of pharmaceutical, nutritional, botanical, and stimulatory therapies, with a discussion of treatment strategies from the perspective of patients and practitioners. Altern Med Rev. 2010; 15:223–44. [PubMed: 21155625]
11. Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev. 2009; 2:270–8. [PubMed: 20716914]

12. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: food sources and bioavailability. Am J Clin Nutr. 2004; 79:727–47. [PubMed: 15113710]
13. Youdim KA, Dobbie MS, Kuhnle G, Proteggente AR, Abbott NJ, Rice-Evans C. Interaction between flavonoids and the blood-brain barrier: in vitro studies. J Neurochem. 2003; 85:180–92. [PubMed: 12641740]
14. Ng TP, Chiam PC, Lee T, Chua HC, Lim L, Kua EH. Curry consumption and cognitive function in the elderly. Am J Epidemiol. 2006; 164:898–906. [PubMed: 16870699]
15. Quideau S, Deffieux D, Douat-Casassus C, Pouységu L. Plant polyphenols: chemical properties, biological activities, and synthesis. Angew Chem Int Ed Engl. 2011; 50:586–621. [PubMed: 21226137]
16. Williams CM, El Mohsen MA, Vauzour D, Rendeiro C, Butler LT, Ellis JA, Whiteman M, Spencer JP. Blueberry-induced changes in spatial working memory correlate with changes in hippocampal CREB phosphorylation and brain-derived neurotrophic factor (BDNF) levels. Free Radic Biol Med. 2008; 45:295–305. [PubMed: 18457678]
17. Spencer JP. The impact of flavonoids on memory: physiological and molecular considerations. Chem Soc Rev. 2009; 38:1152–61. [PubMed: 19421586]
18. Bouayed J, Rammal H, Dicko A, Younos C, Soulimani R. Chlorogenic acid, a polyphenol from Prunus domestica (Mirabelle), with coupled anxiolytic and antioxidant effects. J Neurol Sci. 2007; 262:77–84. [PubMed: 17698084]
19. Huang Z, Zhong XM, Li ZY, Feng CR, Pan AJ, Mao QQ. Curcumin reverses corticosterone-induced depressive-like behavior and decrease in brain BDNF levels in rats. Neurosci Lett. 2011; 493:145–8. [PubMed: 21334417]
20. Delgado PL. Depression: the case for a monoamine deficiency. J Clin Psychiatry. 2000; 61(Suppl 6):7–11. [PubMed: 10775018]
21. Kulkarni SK, Bhutani MK, Bishnoi M. Antidepressant activity of curcumin: involvement of serotonin and dopamine system. Psychopharmacology (Berl). 2008; 201:435–42. [PubMed: 18766332]
22. Kuriyama S, Hozawa A, Ohmori K, Shimazu T, Matsui T, Ebihara S, Awata S, Nagatomi R, Arai H, Tsuji I. Green tea consumption and cognitive function: a cross-sectional study from the Tsurugaya Project 1. Am J Clin Nutr. 2006; 83:355–61. [PubMed: 16469995]
23. Niu K, Hozawa A, Kuriyama S, Ebihara S, Guo H, Nakaya N, Ohmori-Matsuda K, Takahashi H, Masamune Y, Asada M, Sasaki S, Arai H, Awata S, Nagatomi R, Tsuji I. Green tea consumption is associated with depressive symptoms in the elderly. Am J Clin Nutr. 2009; 90:1615–22. [PubMed: 19828710]
24. Hassaninasab A, Hashimoto Y, Tomita-Yokotani K, Kobayashi M. Discovery of the curcumin metabolic pathway involving a unique enzyme in an intestinal microorganism. Proc Natl Acad Sci USA. 2011; 108:6615–20. [PubMed: 21467222]
25. Xu Y, Ku B, Tie L, Yao H, Jiang W, Ma X, Li X. Curcumin reverses the effects of chronic stress on behavior, the HPA axis, BDNF expression and phosphorylation of CREB. Brain Res. 2006; 1122:56–64. [PubMed: 17022948]
26. Wu A, Ying Z, Gomez-Pinilla F. Dietary curcumin counteracts the outcome of traumatic brain injury on oxidative stress, synaptic plasticity, and cognition. Exp Neurol. 2006; 197:309–17. [PubMed: 16364299]
27. Chen WQ, Zhao XL, Hou Y, Li ST, Hong Y, Wang DL, Cheng YY. Protective effects of green tea polyphenols on cognitive impairments induced by psychological stress in rats. Behav Brain Res. 2009; 202:71–6. [PubMed: 19447283]
28. Zhou Z, Hong EJ, Cohen S, Zhao WN, Ho HY, Schmidt L, Chen WG, Lin Y, Savner E, Griffith EC, Hu L, Steen JA, Weitz CJ, Greenberg ME. Brain-specific phosphorylation of MeCP2 regulates activity-dependent Bdnf transcription, dendritic growth, and spine maturation. Neuron. 2006; 52:255–69. [PubMed: 17046689]
29. Li Q, Zhao HF, Zhang ZF, Liu ZG, Pei XR, Wang JB, Cai MY, Li Y. Long-term administration of green tea catechins prevents age-related spatial learning and memory decline in C57BL/6J mice by regulating hippocampal cyclic amp-response element binding protein signaling cascade. Neuroscience. 2009; 159:1208–15. [PubMed: 19409206]

30. Feng L, Gwee X, Kua EH, Ng TP. Cognitive function and tea consumption in community dwelling older Chinese in Singapore. J Nutr Health Aging. 2010; 14:433–8. [PubMed: 20617284]

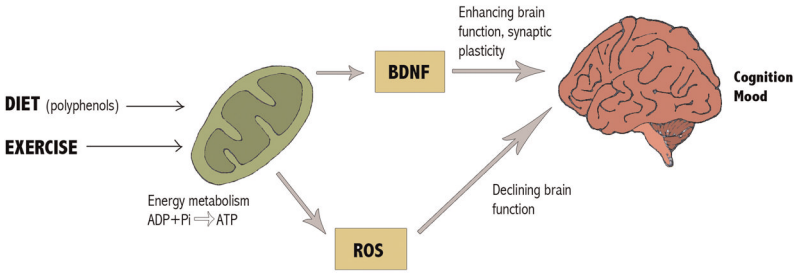

Figure 1.

Energy metabolism and cognition. Diet and exercise can affect cellular metabolic activity, which can influence neuronal plasticity and cognitive processes. It is possible that ATP produced by energy metabolism activates BDNF, a molecule that enhances synaptic plasticity. Energy production also generates oxidative by-products, known as ROS, which in overwhelming amounts can lead to oxidative stress. Oxidative stress weakens synaptic plasticity and cognitive function.

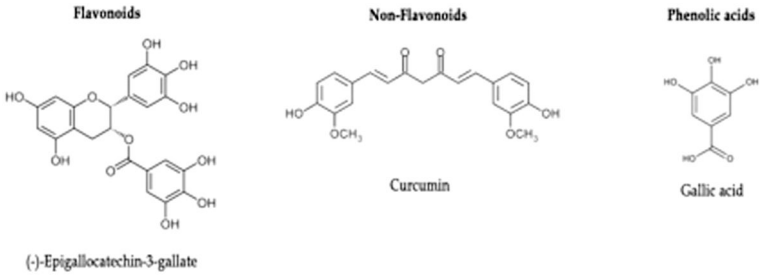

Figure 2.

Structure of polyphenols. Polyphenols can be divided into three categories: flavonoids, non-flavonoids, and phenolic acids. Found in shades of yellow, orange, and red, flavonoids are ketone-containing compounds that are comprised of many subgroups including flavonols, dihydroflavonols, flavones, isoflavones, and flavanones. Non-flavonoids have a different chemical structure from flavonoids and are commonly found in red wines. Phenolic acids consist of a phenolic ring and a carboxylic acid. Examples of each category are pictured.

Table 1

List of polyphenols

Polyphenols	Food sources
Flavonoids	
Catechins	Green and white tea, grapes, cocoa, lentils, berries
Flavanones	Oranges, grapefruit, lemon
Flavanols	Green vegetables, apples, berries, onions
Anthocyanins	Berries, red grapes, wine
Non-flavonoids	
Reservatrol	Grape skin, red wine, nuts
Curcumin	Turmeric, mustard
Coumarin	Licorice, strawberries, apricots, cherries, cinnamon
Phenolic acids	
Ellagic acid	Walnuts, strawberries, cranberries, blackberries, guava, grapes
Tannic acid	Nettles, tea, berries
Gallic acid	Tea, mango, strawberries, rhubarb, soy
Caffeic acid	Blueberries, kiwis, plums, cherries, apples

A list of natural polyphenols found in various food sources. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: food sources and bioavailability. Am J Clin Nutr 2004;79:727-47.