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Review

Brain Neurotrophins and Plant Polyphenols: A Powerful Connection

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Abstract: Neurodegenerative disorders, mental conditions, and cognitive decline represent significant challenges worldwide, with growing pieces of evidence implicating alterations in neurotrophin signaling as central to these diseases. Neurotrophins—such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF)—are indispensable for neuronal survival, differentiation, and synaptic plasticity, and their dysregulation is closely associated with various neuropathological situations. Similarly, dietary plant polyphenols, abundant in vegetables, fruits, wine, tea, and extra virgin olive oil, show powerful anti-inflammatory, antioxidant, and anti-apoptotic activities. This narrative review critically addresses the evolving body of evidence that links plant polyphenols and brain neurotrophins, emphasizing several molecular mechanisms by which polyphenols regulate and modulate neurotrophin signaling. Crucial pathways include mitigation of neuroinflammatory responses, activation of intracellular cascades such as the cAMP response element-binding protein (CREB), epigenetic modulation, and the diminution of oxidative stress. Together, these effects contribute to potentiated enhanced synaptic function, neuronal integrity, and better learning and memory processes. Moreover, this narrative review examines how polyphenol-induced upregulation of neurotrophins may alleviate conditions associated not only with neurodegeneration but also with addiction and mood disorders, suggesting extensive therapeutic approaches. Findings from clinical investigations and animal models are presented to sustain the neuroprotective role of polyphenol-rich diets. Lastly, future research directions are recommended, focusing on polyphenol bioavailability optimization, considering combinatory dietary stratagems, and proposing personalized nutritional interventions. This wide-ranging perspective highlights plant polyphenols as encouraging modulators of neurotrophin pathways and supports their inclusion in approaches aimed at promoting brain health and counteracting neurodegenerative decline.

Keywords: NGF; BDNF; polyphenols; Trk; addiction; curcumin; quercetin; resveratrol; hydroxytyrosol; EGCG; cocoa polyphenols

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1. Introduction

Neurodegenerative diseases, mental disorders, and cognitive decline are among the most persistent health problems all over the world. These disorders not only affect millions of individuals worldwide but also place a significant affliction on caregivers and healthcare systems [1–12]. Brain health is influenced by multiple factors, including lifestyle choices, environmental exposures, and genetic predisposition [13–24]. Among the endogenous factors that regulate neuronal differentiation, survival, and synaptic plasticity, neurotrophins play a pivotal role [25–36]. These peptides, including nerve growth factor (NGF), brain-derived

neurotrophic factor (BDNF), and others, are crucial for maintaining cognitive function and protecting against neurodegeneration [37–39]. They sustain the growth, survival, and maintenance of neuronal cells, and their dysregulation has been associated with various neurological conditions [26,40–46].

Similarly, dietary components, especially plant-derived polyphenols, have gathered important interest due to their putative neuroprotective effects [47–56]. Polyphenols, which are abundant in vegetables, tea, wine, fruits, and other plant-based foods, display a wide range of biological activities. These include antioxidant, anti-inflammatory, and anti-apoptotic properties, which contribute to their protective effects on brain health [57–64]. Pieces of evidence suggest that polyphenols regulate neurotrophin signaling, thus influencing brain functioning and opposition against neurodegenerative disorders. This regulation arises through several mechanisms, such as activating signaling pathways, enhancing neurotrophin expression, and protecting neurons from oxidative stress and inflammation [65–67].

This narrative review aims to explore the connection between brain neurotrophins and plant polyphenols, offering insights into their combined potential for neuroprotection and mental and learning improvements. The understanding of the mechanisms by which neurotrophins and polyphenols cooperate is crucial for developing novel therapeutic approaches. By examining their roles individually and in combination, we can disclose valuable understandings of how dietary interventions may support brain health. This narrative review aims to present a wide-ranging overview of plant polyphenols, and neurotrophins and their synergistic effects on neuroprotection and cognitive function.

Furthermore, the potential therapeutic applications of neurotrophins and polyphenols extend beyond neurodegenerative disorders. Recent studies have highlighted their roles in mental health, suggesting that they may alleviate symptoms of anxiety, depression, and other mood disorders. The interaction between neurotrophins and polyphenols may also play a role in addiction, where neuroplasticity and reward pathways are significantly connected. By exploring these associations, we can better recognize how dietary and lifestyle interventions may participate in mental well-being and addiction recovery.

2. Materials and Methods

In March 2025, a selected literature search was conducted to identify important papers across multiple databases, including PubMed, Scopus, and Web of Science (WOS), to sustain this narrative review. Articles were selected using keywords such as “brain”, “polyphenols”, “neurotrophins”, “animal models”, and “human”, without restriction on publication year. Restricted inclusion criteria were as follows: (1) English-language articles, (2) original studies on brain neurotrophins and polyphenols, and between polyphenols we considered in the discussion resveratrol, epigallocatechin gallate (EGCG), quercetin, curcumin, hydroxytyrosol/oleuropein/tyrosol (olive polyphenols), cocoa polyphenols. Letters, editorials, and case reports were included where appropriate. Studies meeting these criteria were further analyzed, and relevant data were extracted from each paper.

3. Neurotrophins

Neurotrophins are a family of growth factors essential for the development, survival, and function of neurons [68–74]. The principal neurotrophins include nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and neurotrophin-4/5 (NT-4/5) [36,75–79]. These peptides are important for maintaining the health and functionality of the nervous system. Among these, NGF and BDNF are particularly vital for synaptic plasticity, memory, and learning [69,80–82]. The dysregulation

of neurotrophin signaling has been associated with various neurological and psychiatric disorders, including Parkinson's disease, Alzheimer's disease, and depression [26,83–88].

The action of neurotrophins is based on two classes of receptors: tropomyosin receptor kinase (Trk) receptors and the p75 neurotrophin receptor (p75NTR) [89–93]. Trk receptors, including TrkA, TrkB, and TrkC, primarily mediate survival and differentiation signals [93–97]. For instance, TrkA binds NGF, TrkB binds BDNF and NT-4/5, and TrkC binds NT-3. These bonds activate intracellular signaling pathways that promote neuronal growth, survival, and synaptic plasticity. On the other hand, p75NTR can induce apoptosis under certain conditions, particularly when neurotrophin levels are low or when the receptor is unbound [98–103]. This Janus role of neurotrophin receptors underlines the complexity of neurotrophin signaling in brain health.

According to their fundamental role in brain health, approaches aimed at modulating neurotrophin levels and action are of intriguing interest in neuroscience research. Indeed, therapeutic approaches may include the use of peptides, small molecules, and gene therapy to enhance neurotrophin signaling [104–110]. Furthermore, lifestyle interventions such as dietary modifications and physical exercise have been shown to influence neurotrophin levels, offering non-pharmacological avenues for promoting brain health [111–115].

NGF and BDNF, in particular, have been widely studied due to their role in neurogenesis and synaptic plasticity [75,94,116–119]. NGF and BDNF are highly expressed in the hippocampus, cortex, and basal forebrain—regions associated with cognitive function and memory [120–126]. NGF and BDNF expression are regulated by several factors, including physical activity, stress, and diet [127–131]. For example, exercise has been shown to modulate NGF and BDNF levels, which are associated with improved cognitive function and reduced risk of neurodegenerative diseases [132–134]. Stress, on the other hand, can alter NGF and BDNF levels, resulting in cognitive impairment and mood disorders [69,111,135,136]. Significantly, emerging pieces of evidence indicate that dietary polyphenols can modulate NGF and BDNF levels, providing a promising opportunity for cognitive enhancement and neuroprotection [65,137–141].

Previous studies have indicated that NGF and BDNF expression declines with age [142–145], a feature associated with cognitive disruption and increased susceptibility to neurodegenerative conditions. The molecular mechanisms underlying NGF and BDNF modulation include transcriptional control via CREB (cAMP response element-binding protein) [146–149] and connections with neuroinflammatory processes [67,150,151]. Indeed, CREB is a transcription factor that binds to the promoter region of the BDNF gene, enhancing its expression [147,152]. Neuroinflammation, which is quite common in both aging and neurodegenerative disorders, can negatively affect NGF and BDNF signaling, further potentiating cognitive decline [153–157]. Since NGF and BDNF play such a key role in neuronal survival, interventions aimed at modulating their levels, either pharmacologically or dietary interventions, are a focus of current research.

Moreover, animal model studies have shown that genetic knockdown of BDNF leads to severe cognitive deficits, supporting its essential role in brain function [158–165]. By contrast, the upregulation of NGF and BDNF through exercise or dietary modifications has been associated with potentiated synaptic plasticity, suggesting potential therapeutic strategies for neurodegenerative conditions [112–115]. Recent clinical trials exploring the use of BDNF enhancers highlight promising directions in neuromodulation and cognitive therapy [166–170]. Indeed, these trials aimed to disclose safe and effective procedures for boosting neurotrophin levels in humans, with the purpose of improving cognition and reducing the risk of neurodegenerative disorders.

4. Plant Polyphenols

Polyphenols are bioactive compounds found in vegetables, fruits, coffee, tea, wine, and various medicinal plants [54,171–176]. They are classified into different categories, including phenolic acids, flavonoids, lignans, and stilbenes, each showing distinctive biological activities [173,177–179]. Flavonoids, particularly anthocyanins, catechins, and quercetin, are among the most investigated polyphenols in the context of brain health [180,181]. These chemicals are known for their powerful antioxidant properties [173,176,182–184], which support the neutralization of free radicals and counteract oxidative stress—a crucial factor in neurodegeneration.

Polyphenols possess multiple beneficial effects, including neuroprotective antioxidant, and anti-inflammatory properties (Figure 1). They regulate key signaling pathways involved in mitochondrial function, oxidative stress, and neuronal survival [185–189]. For instance, polyphenols can modulate the Nrf2 pathway, which improves the expression of antioxidant enzymes and protects neurons from oxidative damage [190–192].

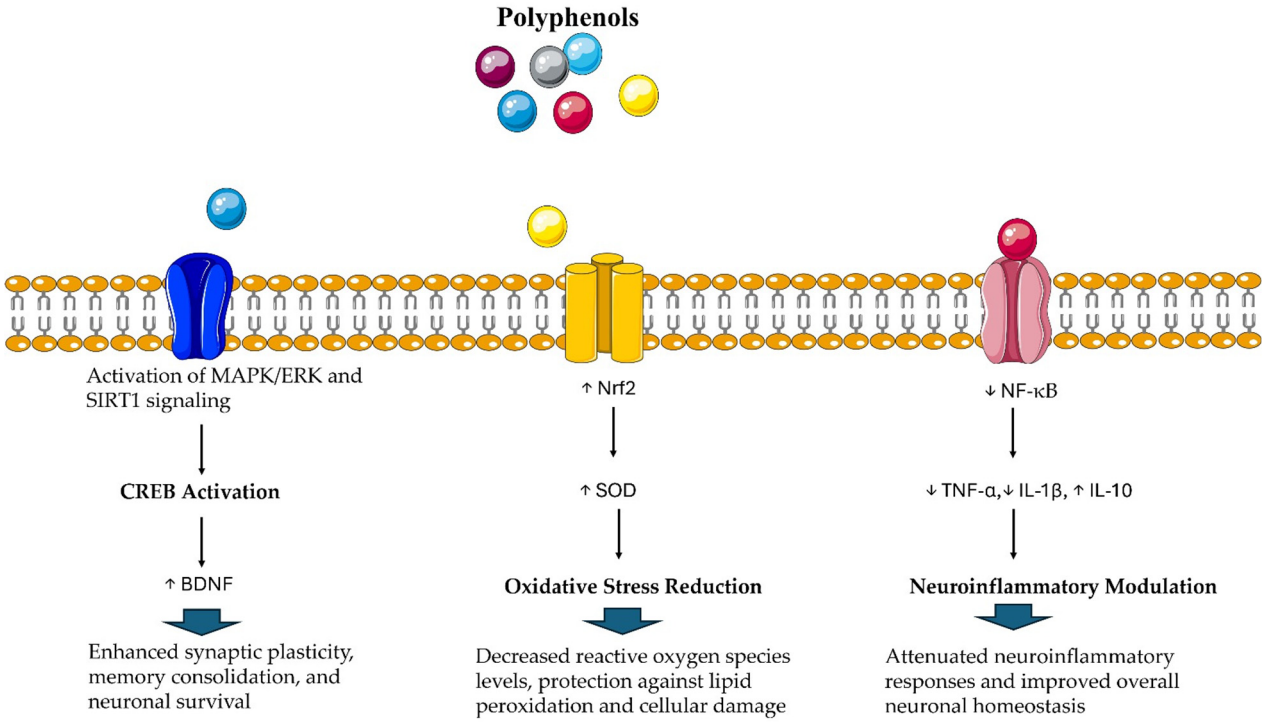

Figure 1. Through distinct biomolecular pathways, polyphenols exert a variety of health-promoting effects, contributing to neuroprotection, antioxidant defense, and the modulation of neuroinflammatory processes. Servier Medical Art by Servier is licensed under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/ accessed on 18 May 2025). ↑ Indicates elevation. ↓ Indicates reduction.

Furthermore, polyphenols can constrain the NF-κB pathway, decreasing inflammation and promoting neuronal health [141,190,192,193]. Particularly, polyphenols can cross the blood–brain barrier (BBB), permitting a direct communication between neuronal circuits and molecular targets within the brain [54,194,195]. This aptitude to breach the BBB is critical for its neuroprotective effects, as it allows polyphenols to act straightforwardly within the central nervous system (Table 1).

Table 1. Proposed biomolecular mechanisms dealing with the multifactorial action of polyphenols. *CREB activation*: polyphenols such as resveratrol and epigallocatechin gallate (EGCG) could stimulate MAPK/ERK and SIRT1 signaling, which in turn phosphorylate CREB and upregulate neurotrophins. This induces synaptic plasticity and sustains learning and memory. *Oxidative stress reduction*: through the activation of the Nrf2 pathway, polyphenols might potentiate the expression of antioxidant factors (e.g., SOD, catalase) that alleviate reactive oxygen species, thus protecting brain cells. *Neuroinflammation modulation*: by reducing the NF-κB pathway, polyphenols could depress the secretion of pro-inflammatory cytokines (e.g., TNF-α, IL-1β), decreasing neuroinflammation and potentially limiting neurodegeneration.

Polyphenols	Proposed Mechanisms	Molecular Pathway/Targets	Biological Outcomes
Resveratrol, epigallocatechin gallate (EGCG), curcumin	CREB activation	- Activation of MAPK/ERK and SIRT1 signaling—Phosphorylation of CREB—Upregulation of BDNF and other neurotrophins	Enhanced synaptic plasticity, memory consolidation, and neuronal survival
EGCG, resveratrol, quercetin	Reduction of oxidative stress	- Direct free radical scavenging—Activation of Nrf2 pathway leading to increased expression of antioxidant enzymes (e.g., SOD, catalase)	Decreased reactive oxygen species levels, protection against lipid peroxidation and cellular damage
Curcumin, resveratrol, hydroxytyrosol (olive polyphenols)	Modulation of neuroinflammatory mediators	- Inhibition of NF-κB signaling—Reduced expression of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6)—Modulation of microglial activity	Attenuated neuroinflammatory responses and improved overall neuronal homeostasis

Among the most potent neuroprotective polyphenols are resveratrol, hydroxytyrosol, curcumin, EGCG, and quercetin. These chemicals have been shown to potentiate neuronal function through several mechanisms, including the activation of the neurotrophic signaling pathways [65,196,197]. Resveratrol, a stilbene commonly found in grapes, red wine, and other plants has been described to modulate synaptic plasticity and Sirtuin 1 (SIRT1) (see Table 1), a longevity-associated protein that interacts with BDNF signaling pathways [141,198–201]. Indeed, SIRT1 activation by resveratrol can potentiate BDNF expression, promoting cognitive function and neuronal survival [202–206]. Curcumin, a bioactive chemical in turmeric, has revealed neuroprotective effects in Alzheimer's animal models by reducing amyloid-beta plaque deposition and elevating BDNF levels [207–209]. Curcumin's anti-inflammatory properties also participate to its neuroprotective actions, since chronic inflammation is a characteristic of neurodegenerative diseases [207–209]. EGCG, found in green tea, has been associated with reduced neuroinflammation and enhanced neurogenesis, eliciting improved cognitive function [210–214]. Indeed, EGCG also regulates mitochondrial function reducing oxidative stress, and enhancing energy production in neurons [215–218].

Quercetin, a flavonoid present in many vegetables and fruits, has been shown to protect neurons from apoptosis and oxidative stress [215–218]. Indeed, quercetin regulates signaling pathways such as mitogen-activated protein kinase (MAPK) and PI3K/Akt [219,220] (see Table 1), which are involved in cell survival and neuroprotec-

tion. The ability of quercetin to boost mitochondrial action and reduce neuroinflammation further emphasizes its putative function in brain health.

A parallel dissertation can be told for hydroxytyrosol. Indeed, hydroxytyrosol and oleuropein are well known for their antioxidant, anti-inflammatory, and neuroprotective properties leading to the counteraction of neurodegenerative diseases of the central/peripheral nervous system, improving adult neurogenesis, senescence, and lifespan [221–224].

In addition to specific polyphenols, dietary applications rich in polyphenols, such as traditional Asian diets and the Mediterranean diet, have been related to enriched cognitive functioning and reduced incidence of neurodegenerative conditions [225–229]. The Mediterranean diet, which embraces high consumption of vegetables, fruits, seeds, nuts, and extra virgin olive oil, is particularly rich in polyphenols (Figure 2).

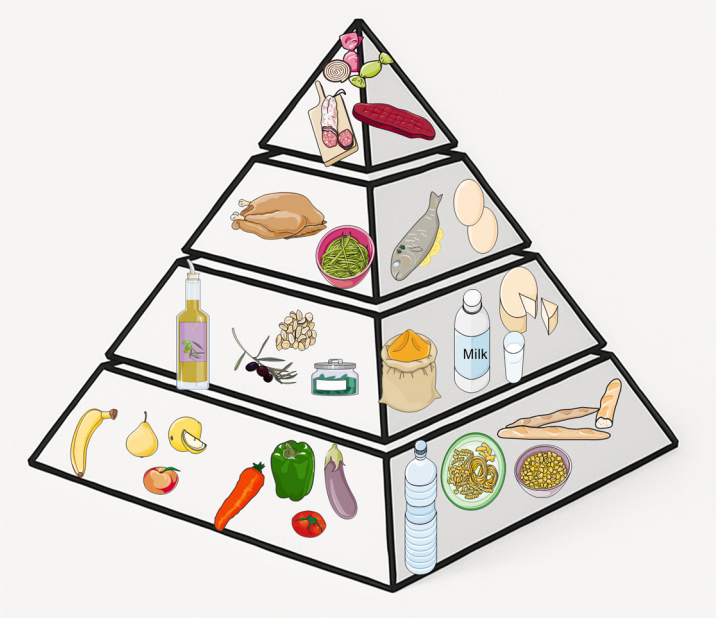

Figure 2. The Mediterranean diet is rich in polyphenols: fruits and vegetables, in particular berries, red grapes and red wine, green and black tea, cocoa, chocolate, olives and extra virgin olive oil. It is suggested to eat at least 2 portions of vegetables in the main meals with 1–2 portions of fruits and cereals. Nuts, seeds and olives (1–2 servings), but also milk and dairy products (2–3 servings), herbs and spices and olive oil (3–4 servings) should be consumed daily. Finally, weekly consumption of fish, crustaceans and mollusks (at least 2 servings), poultry (1–2 servings), eggs (2–4 servings) and legumes (at least 2 servings) is indicated. Meat, sweets, and cold cuts should be eaten sparingly (no more than 1 time a week). Water should be the main drink, but moderate consumption of wine is permitted. Servier Medical Art by Servier is licensed under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/ accessed on 18 May 2025).

Studies have disclosed that adherence to the Mediterranean diet is associated with better cognitive function and a lower risk of brain aging [230–234]. Similarly, traditional Asian diets, which involve soy products, green tea, and several herbs, offer a rich source of polyphenols that participate to brain health [231,232,235].

Clinical studies indicate that long-term consumption of polyphenol-rich foods contributes to improved neuronal resilience and better brain aging against stress-related damage. For example, studies on elderly individuals disclosed that regular consumption of polyphenol-rich foods was associated with improved cognitive performance and a lower risk of cognitive decline [166,236–239]. These conclusions highlight the impor-

tance of dietary polyphenols in preventing neurodegenerative diseases and maintaining brain health.

5. Polyphenols and the Gut–Brain Axis

Polyphenols may also have a role in regulating gut–brain interactions [240–243]. Indeed, the gut microbiota can absorb polyphenols into bioactive metabolites that can cross the blood–brain barrier, influencing brain function. For example, polyphenols can promote the growth of beneficial gut bacteria that produce short-chain fatty acids (SCFAs), which have been shown to influence brain function and reduce inflammation [244,245].

Indeed, beyond their straight actions in the central nervous system (CNS), plant polyphenols greatly reshape the gut microbiota environment, modulating bioactive metabolites affecting brain functions [246]. In the colon, unabsorbed polyphenols undertake extensive modifications by resident bacteria into SCFAs and low-molecular-weight phenolic acids, which present enriched blood–brain barrier permeability and intestinal absorption. By acting as a sort of prebiotics, polyphenols selectively enrich SCFA-producing taxa (e.g., *Faecalibacterium* sp., *Roseburia* sp.) and beneficial bifidobacteria and lactobacilli while reducing pathobionts. This transformed microbiome not only elevates systemic levels of propionate, butyrate, and acetate but also could modulate circulating indole derivatives and tryptophan, important precursors for brain neurotrophins and neuromodulators [246].

As for SCFAs, they serve as molecular messengers of the microbiota–gut–brain axis by linking free-fatty-acid receptors on enteroendocrine cells and vagal afferents [247], and by acting on microglia throughout the SCFA–microglia pathway [247]. Indeed, butyrate acts as a histone deacetylase inhibitor in the CNS, leading to epigenetic inhibition of NGF/BDNF gene promoters in the hippocampus [247]. This elicits CREB activation and neurotrophin release, increasing synaptic plasticity and counteracting inflammation. Concomitantly, microbial phenolic metabolites, (i.e., urolithins and p-coumaric acid) might exert anti-inflammatory actions on gut-associated lymphoid tissue, reducing peripheral cytokine release that could compromise neurotrophin signaling within the blood–brain barrier [246].

Animal and human data highlight that polyphenols-rich long-term dietary patterns (e.g., Mediterranean, plant-forward diets) correlate with higher plasma and CSF levels of BDNF, SCFA-enriched microbiota, and better cognitive performance during aging [241,248]. Thus, the integration of prebiotic modulation with potentiated microbial populations could elicit the release of neuroactive small molecules, and epigenetic upregulation of neurotrophin pathways to further underscore the subtle polyphenols' role in a multidimensional gut–brain axis mechanism [240–243].

6. Brain and Plant Polyphenols

Recent research focuses on the aptitude of plant polyphenols to potentiate neurotrophin signaling and expression. Many studies show that polyphenol-rich diets may increase NGF and BDNF levels, promoting cognitive function and brain cells' resilience. Several biomolecular mechanisms support this feature:

6.1. Epigenetic Modulation

Polyphenols can modify gene expression through DNA methylation and histone modification [249–254], modulating neurotrophin synthesis and release. For example, curcumin and resveratrol have been shown to affect histone acetylation, leading to elevated expression of BDNF [255–258]. These epigenetic modifications can have long-lasting effects on brain function and neuronal plasticity. Furthermore, polyphenols can influence DNA methylation configurations [259–261], which play a subtle role in modulating gene

expression. Thus, by regulating these epigenetic mechanisms, polyphenols can increase the synthesis of neurotrophins and promote neuronal health.

6.2. Activation of Cellular Pathways

Polyphenols trigger pathways such as cAMP response element-binding protein (CREB), which is crucial for the transcription of NGF and BDNF [138,262]. CREB is a key transcription factor that, when activated, binds to the promoter region of the BDNF gene, potentiating its expression [263,264]. Quercetin and EGCG have been shown to activate CREB through various signaling cascades, including the MAPK/ERK and PI3K/Akt pathways [265,266] (see Table 1). These pathways play a role in cell differentiation, survival, and synaptic plasticity, emphasizing the multifaceted role of polyphenols in brain functions.

6.3. Mitigation of Neuroinflammation

By dropping inflammatory cytokines, polyphenols may prevent neurotrophin deprivation and improve their protective effects [176,267–270]. Chronic inflammation is a crucial factor in neurodegenerative conditions, and polyphenols can prevent the synthesis and release of pro-inflammatory cytokines such as TNF-α and IL-1β [271–275] (see Table 1). This anti-inflammatory achievement supports preserving neurotrophin levels, inducing neuronal health. Furthermore, polyphenols can modulate the activity of microglia [47,276,277], the brain's resident immune cells, decreasing their pro-inflammatory reactions and stimulating a neuroprotective environment.

6.4. Oxidative Stress Reduction

Polyphenols may reduce oxidative stress [239,276,278,279], maintaining neuronal integrity and supporting the neurotrophin role. Indeed, oxidative and nitrosative stresses are major contributors to neuronal damage and neurodegeneration. Polyphenols, throughout their solid antioxidant properties, can counteract free radicals and modulate endogenous antioxidant defenses, thus protecting neurons and eliciting neurotrophin signaling. For example, polyphenols can enhance the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase [280–282], which have a key role in sustaining cellular redox balance.

6.5. Model Studies

Studies on animal models and human subjects support the role of polyphenols in cognitive enhancement. For example, flavonoid-rich diets have been associated with improved memory and learning capabilities [283,284]. In animal models, polyphenols supplementation such as cocoa, green tea, and blueberries has been shown to potentiate cognition and elevate hippocampal BDNF [285–288]. These findings indicate that dietary polyphenols may modulate brain resilience and function by enhancing synaptic plasticity, which is crucial for learning and memory processes.

Furthermore, several studies have suggested that people consuming polyphenol-rich diets (such as fruits, vegetables, and tea) demonstrate a reduced risk of neurodegenerative disorders [289–291]. These observational investigations provide convincing evidence for the protective effects of polyphenols on brain health, also through their effects on the gut–brain axis [244,246,292].

Clinical trials have provided additional indications of the neuroprotective effects of polyphenols. A previous study on elderly people consuming a Mediterranean diet rich in polyphenols revealed enriched cognitive performance and elevated plasma BDNF [293]. Additionally, randomized controlled trials on polyphenol supplementation have reported benefits in delaying cognitive decline in patients with mild cognitive impairment [139,294–296].

Indeed, supplementation with curcumin, resveratrol, or EGCG improved cognitive tasks and elevated BDNF levels in clinical individuals [139,294–296] (Table 2).

Table 2. Polyphenol regulation of neurotrophin receptors and signaling pathways. This table presents an overview of how various polyphenols interact with neurotrophin receptors (TrkA, TrkB) and crucial molecular pathways involved in neuroprotection, synaptic plasticity, and neuronal survival. Resveratrol, epigallocatechin gallate (EGCG), curcumin, quercetin, and hydroxytyrosol have been shown to regulate neurotrophins such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), affecting pathways including PI3K/Akt signaling, CREB phosphorylation, and NF-κB inhibition. These biomolecular processes participate in potentiated neuronal resilience, improved memory and learning processes, and a protective action against neurodegeneration. Experimental models, ranging from in vitro neuronal cultures to in vivo investigations on neurodegenerative conditions (Alzheimer's, Parkinson's, and addiction models), sustain the neurotrophic-potentiating actions of polyphenols. ↑ Indicates elevation.

Polyphenol	Targeted Neurotrophins/Receptors	Signaling Pathways Affected	Neurological Effects	Experimental Models
Resveratrol	BDNF, NGF, TrkB, TrkA	-↑ CREB phosphorylation—Activation of PI3K/Akt and ERK cascade	Improves memory, enhances synaptic plasticity	Rodent models, in vitro neuronal culture studies
EGCG (green tea)	BDNF, TrkB	-↑ BDNF expression—Suppression of NF-κB-driven inflammation	Protects neurons from oxidative stress, reduces apoptosis	Mouse models of cognitive dysfunction, aging studies
Curcumin	NGF, BDNF, TrkA, TrkB	- Modulates NF-κB—↑ Anti-apoptotic Bcl-2 pathways	Enhances neurogenesis, prevents inflammation	Parkinson's and Alzheimer's animal studies
Quercetin	BDNF, NGF	-↑ MAPK/ERK signaling—Regulates neurotrophin transcription factors	Enhances neuronal resilience, neuroprotection	In vitro hippocampal neuron models
Hydroxytyrosol (olive polyphenols)	NGF, BDNF, TrkA, TrkB	- Increases NGF synthesis—Regulates mitochondrial oxidative metabolism	Supports neuronal survival, counters neurodegeneration	Preclinical models of Alzheimer's and aging disorders

As for cocoa polyphenols, a randomized, double-blind, parallel-group study on 60 healthy volunteers between 50 and 75 years old who consumed a cocoa powder, a red berries mixture or a combination of both for 12 weeks it was shown an improvement in executive function without significant difference in BDNF and NGF-receptor sera levels [297]. In an Alzheimer in vitro study, cocoa powder triggers neuroprotective and preventive effects by modulating BDNF signaling pathway [298], whereas a diet enriched with high-phenolic cocoa potentiates hippocampal brain-derived neurotrophic factor expression and neurogenesis in healthy adult mice with subtle effects on memory [285].

Another study examined the effects of dark chocolate intake on improving brain function during cognitive tasks using functional magnetic resonance imaging (fMRI) [238]. In this randomized, single-blinded, crossover, and dose-comparison study, 26 healthy middle-aged participants ingested dark chocolate (25 g) either with a low concentration (LC) (211.7 mg) or a high concentration (HC) (635 mg) of cacao polyphenols (mainly epicatechin and theobromine) [238]. Thereafter, their brain activities were analyzed during continuous and effortful cognitive tasks relevant to executive functioning using fMRI

in two consecutive 15 min sessions (25 and 50 min after ingestion) [238]. The authors observed significant interaction effects between chocolate consumption and brain activity measurement sessions in the left dorsolateral prefrontal cortex and left inferior parietal lobule [238].

7. Polyphenols, Neurotrophins, and Addiction

Addiction is a multifaceted disorder involving dysregulation of neurochemical pathways, particularly those associated with neuroplasticity and reward processing [299–301]. Chronic abuse of addictive substances such as nicotine, alcohol, and drugs alters neurotrophin levels, particularly NGF and BDNF [302]. The dysregulation of NGF and BDNF and other neurotrophins contributes to the neuroadaptive changes, including alterations in synaptic connectivity and strength in brain areas involved in motivation and reward [69,303,304].

Plant polyphenols have been studied for their putative role in mitigating addiction-related neuroadaptations. Indeed, several studies, mostly in animal model studies, suggest that polyphenols can modulate neurotransmitter signaling and neurotrophin presence, which both have a critical role in the brain's reward structure. For example:

7.1. Resveratrol

Resveratrol has been shown to reduce drug-seeking behavior by enhancing BDNF levels and modulating dopamine receptor expression in addiction-related brain regions [305–307]. Indeed, resveratrol's capability to modulate the dopaminergic system is particularly significant [308–310], as dopamine has a key role in the reward circuitry and the reinforcing effects of abuse substances. Further, in a mouse model, the consumption of resveratrol through metabolite formation may have a protective role by reducing free radical presence and tempering the BDNF involved in hepatic disruption induced by chronic alcohol abuse [197,311,312].

7.2. Curcumin

Curcumin shows neuroprotective actions in addiction models by dropping inflammation and oxidative stress, which participate in relapse vulnerability [313–316]. Indeed, chronic exposure to substance abuse often leads to elevated neuroinflammation and oxidative stress, which can harm neurons and damage cognitive function. Thus, curcumin's anti-inflammatory and antioxidant properties could mitigate these effects, supporting neuronal health and reducing the possibility of relapse. Curcumin has been also shown to regulate neurotransmitter systems, including dopamine and serotonin, which are both involved in abuse dependence and mood modulation [317–319].

7.3. Green Tea Polyphenols

Green tea polyphenols, particularly EGCG, have demonstrated the ability to modulate withdrawal symptoms [320] and normalize neurotrophin expression [321–325]. Indeed, withdrawal from abuse substances can lead to a variety of outcomes, including depression, anxiety, and cognitive changes. EGCG's neuroprotective actions could alleviate these symptoms by potentiating neurotrophin signaling and stimulating neuronal recovery. Furthermore, EGCG has been shown to regulate the activity of the dopamine system [326,327], which has a key role in the rewarding drug effects [328,329].

7.4. Olive Polyphenols

Oleuropein, tyrosol, and hydroxytyrosol, obtained from the olive plant leaves and seeds, have also shown potential in substance abuse research. Hydroxytyrosol and tyrosol, found in olive oil and extra virgin olive oil, show strong anti-inflammatory and

antioxidant abilities [330]. These polyphenols are known to protect neurons from oxidative stress [331,332], enhance neurotrophin signaling [65,137,197,333], and potentially modulate the neurotoxic effects of addictive substances [334]. Oleuropein, another olive polyphenol, shows neuroprotective actions by regulating dopamine signaling and reducing neuroinflammation [335–339]. Quite interestingly, hydroxytyrosol is also known as DOPET (3,4-dihydroxy-phenylethanol), a well-known dopamine metabolite, and is known to be endogenously secreted and present in mammal body fluids at low concentrations [340,341], further supporting the key role of hydroxytyrosol in the addiction/reward systems.

8. Discussion and Conclusions

The association between plant polyphenols and neurotrophins offers a promising opportunity for neuroprotection and cognitive potentiation. Based on the increasing prevalence of neurodegenerative diseases associated with aging and cognitive deterioration, modifications in dietary approaches could enhance neurotrophin activity offering non-invasive accessible interventions. These strategies are particularly attractive since they can be easily incorporated into daily life and have the potential to boost brain health without the necessity for pharmaceutical interventions.

Future research should focus on clarifying the detailed molecular mechanisms through which polyphenols modulate neurotrophin signaling. The comprehension of these mechanisms will be crucial for developing directed dietary interventions and therapeutic strategies. For instance, disclosing specific polyphenols that most successfully potentiate neurotrophin signaling and expression might lead to the development of supplements or functional foods intended to sustain brain health. Of course, additional research should explore how polyphenols interact with other dietary components and lifestyle factors that might influence neurotrophin activity.

Clinical investigations are necessary to establish optimal dosages, bioavailability, and long-term effects of polyphenol-rich diets. These studies should aim to determine international evidence-based guidelines for polyphenol consumption to optimize their neuroprotective benefits. Indeed, factors such as genetic background, age, sex, and pre-existing health conditions could have a role in the effectiveness of polyphenol interventions, and personalized approaches could be necessary to obtain the best outcomes. Moreover, long-term studies are indispensable to assess the safety and sustainability of polyphenol-rich diets over extended times.

It should also be noted that investigating the cooperative interactions between different polyphenols and other bioactive compounds could improve their neuroprotective ability. For instance, combining polyphenols with vitamins, omega-3 fatty acids, or minerals could elicit additive or synergistic outcomes that further sustain brain health [342–344]. Exploring this synergistic supplementation could disclose comprehensive dietary strategies that might raise cognitive function and protect against neurodegenerative disorders.

The ability of polyphenols to regulate neurotrophins is not static but differs noticeably with both the dose and duration of supplementation. Acute interventions often induce prompt, transient spikes in circulating and central neurotrophin levels, while chronic schedules are required to maintain and strengthen these modifications.

In healthy volunteers, *acute* doses of cocoa flavanols elicited a rise in serum BDNF [345,346]. Similarly, EGCG in mice increased hippocampal BDNF mRNA [347]. Long-lasting supplementation (4–12 weeks) is often required to achieve durable neurotrophic upregulation: in older adults, daily consumption of circa 500 mg cocoa flavanols for 12 weeks raised resting plasma BDNF and improved performance on memory tasks [348]. Rodent studies likewise show that resveratrol elevates hippocampal BDNF expression [349] and modulates dendritic spine density [350], whereas a single dose has debated effects.

These observations emphasize the necessity for cautious titration of polyphenol assumption to balance pro-neurotrophic signaling against metabolic clearance and/or potential pro-oxidant effects at supraphysiological concentrations [351,352].

However, although several papers evidenced the effects of polyphenols on neurotrophin synthesis and release, some clinical trials in aged people failed to disclose significant changes in circulating neurotrophins following polyphenol administration [139]. For instance, 12 weeks of supplementation with cocoa flavanols in cognitively healthy elderly subjects found no modifications in plasma BDNF levels versus the placebo group [297]. Similarly, it was observed that curcumin administration in amateur long-distance runners did not significantly change serum BDNF [294]. Such inconsistencies probably suggest heterogeneity in polyphenol source, assay sensitivity, duration, dose, and baseline nutritional and health status emphasizing the need for larger trials.

Despite the promising discoveries, several unresolved questions remain. The polyphenols bioavailability differs significantly depending on their chemical structure, concentration, and metabolic pathways. Polyphenols may be metabolized quickly or may have limited absorption in the gastrointestinal tract, decreasing their efficacy. According to this issue, approaches to improve their absorption and stability, such as dietary co-administration and nanoencapsulation, should be investigated [353–357]. To improve polyphenol stability, encapsulating polyphenols in nanoparticles could be considered to reduce degradation and improve their absorption too. Co-administration with other dietary elements, such as proteins or fats, could also enhance polyphenol bioavailability. For instance, curcumin displays important challenges due to its poor aqueous solubility (<0.1 mg/mL), low oral bioavailability (often below 1%), and rapid metabolism into sulfate and glucuronide conjugates, leading to low blood–brain barrier penetration [358–361]. These factors limit its therapeutic potential, particularly with oral administration. However, these limits have encouraged research into approaches aimed to improve curcumin's bioavailability, including methods such as liposomes, nanoparticles, or co-administration with piperine (found in black pepper, that may inhibit glucuronidation and increase curcumin's bioavailability) [362,363].

As for the Janus face of microglia and macrophages in neuroinflammation, it should be noted that microglia and infiltrating blood-derived macrophages show amazing phenotypic plasticity, swinging between neuroprotective and neurotoxic states depending on local signs. In their classic ("M2-like") mode, they remove debris, release anti-inflammatory cytokines (e.g., TGF-β, IL-10) and may produce BDNF and NGF to sustain neuronal survival and synaptic remodeling [364–366]. On the contrary, chronic exposure to danger-associated molecular circuits or pro-inflammatory cues, they adopt a classic "M1-like" profile [367], releasing IL-1β, TNF-α, reactive oxygen species and nitric oxide that can disrupt neurotrophin signaling and aggravate neuronal damage [365,368].

Transcriptomics investigations disclosed a wide spectrum of intermediate activation conditions beyond this dualistic classification [369,370], including disease-associated microglia that could firstly constrain pathology but, under certain circumstances, participate in synaptic loss and demyelination [368]. Thus, the comprehension of how plant polyphenols regulate this delicate equilibrium, shifting microglia/macrophages toward anti-inflammatory, neurotrophin-releasing phenotypes, will be significant for disclosing their complete therapeutic potential in neuropsychiatric and neurodegenerative conditions.

A descriptive study on the influence of polyphenol supplementation and exercise on depression and brain function parameters examined the combined antidepressant effects of exercise and polyphenol supplementation, with a special focus on specific polyphenolic chemicals such as curcumin, crocin, and quercetin, as well as different methods of physical exercise, including resistance and aerobic training [371]. Indeed, these interventions modulate cognitive function, depressive-like behaviors, and neurochemical biomarkers in animal

models and humans [371]. The findings disclosed that both polyphenols and exercise independently participate in reduced anxiety, mood enhancement, and improved cognitive function through mechanisms such as neurotransmitter modulation, neurogenesis, and anti-inflammatory effects [371]. Intriguingly, the combined interventions showed a synergistic effect, providing significant health benefits in decreasing symptoms of depression and anxiety, enhancing cognitive processes, and supporting overall mental well-being [371].

In conclusion, the relationship between plant polyphenols and neurotrophins embodies a compelling field of investigation with important implications for brain function and disease prevention. Diets rich in polyphenol-containing foods may act as an effective and practical strategy to sustain learning and memory functions, modulating neurodegenerative processes. Indeed, the potential benefits of polyphenols cover beyond neuroprotection, as they may also reduce anxiety, support mood, and improve overall mental well-being. Future research should decode these findings into clinical applications, paving the way for polyphenol-based neuroprotective interventions. By disclosing evidence-based guidelines and investigating novel delivery methods, we could exploit the influence of polyphenols in promoting brain health and preventing learning and memory decline.

Likewise, interdisciplinary collaborations could be indispensable to make advancements in this field. Investigators from clinical medicine, neuroscience, nutrition, and pharmacology should collaborate to propose comprehensive research that addresses the complex association between neurotrophins, brain health, and diet. Public health initiatives should also promote the understanding of the benefits of polyphenol-rich diets and support their acceptance as a crucial portion of a healthy lifestyle.

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Abbreviations

The following abbreviations are used in this manuscript:

BBB	Blood–brain barrier
BDNF	Brain-derived neurotrophic factor
CREB	cAMP response element-binding protein
DOPET	3,4-dihydroxy-phenylethanol
EGCG	Epigallocatechin gallate
MAPK	Mitogen-activated protein kinase
NGF	Nerve growth factor
Nrf2	Nuclear factor erythroid 2-related factor 2
NT-3	Neurotrophin-3
NT-4/5	Neurotrophin-4/5

p75NTR	p75 neurotrophin receptor
SCFAs	Short-chain fatty acids
SIRT1	Sirtuin 1
SOD	Superoxide dismutase
Trk	Tropomyosin receptor kinase
WOS	Web of Science

References

1. Han, A.; Oster, R.; Yuen, H.; Jenkins, J.; Hawkins, J.; Edwards, L. Videoconference-Delivered Acceptance and Commitment Therapy for Family Caregivers of People with Dementia: Pilot Randomized Controlled Trial. *JMIR Form. Res.* **2025**, *9*, e67545. [CrossRef] [PubMed]
2. Carlo, L.; Carlo, M.P.J.; O'Donnell, A.; Estrada, L.V. Technology-Based Mental Health Interventions in Dementia Care: A Systematic Review. *J. Gerontol. Nurs.* **2025**, *51*, 19–28. [CrossRef] [PubMed]
3. van Husen, G.; Burger, T.J.; de Koning, M.B.; de Wit, M.A.S.; Segeren, M.W.; Beekman, A.T.F. Needs of the network: A qualitative study of the needs of family members, partners and close friends of people with a severe mental illness (SMI). *BMC Psychiatry* **2025**, *25*, 220. [CrossRef]
4. Weerasinghe, T.; Dassanayake, R.; Senapathy, M.; Thennakoon, R.; Dayasiri, K. The role of primary caregivers' knowledge, attitudes, and practices in paediatric medication safety. *BMC Res. Notes* **2025**, *18*, 94. [CrossRef] [PubMed]
5. Teoh, Y.; Garg, P.; Karyadiguna, N.; Vivekanandarajah, S.; So, L.; Hurwitz, R.; Raman, S. Caregiver experiences of accessing a child developmental assessment service in a culturally diverse population in Australia: A mixed methods study. *BMJ Paediatr. Open* **2025**, *9*, e003003. [CrossRef]
6. Scharf, A.; Michalowsky, B.; Rädke, A.; Kleinke, F.; Schade, S.; Platen, M.; Buchholz, M.; Pfaff, M.; Iskandar, A.; van den Berg, N.; et al. Identifying and Addressing Unmet Needs in Dementia: The Role of Care Access and Psychosocial Support. *Int. J. Geriatr. Psychiatry* **2025**, *40*, e70066. [CrossRef]
7. Mao, J.; Yamakawa, M.; Hu, X.; Chikama, H.; Swa, T.; Takeya, Y. Negative Consequences of Sleep Deprivation Experienced by Informal Caregivers of People With Dementia on Caregivers and Care Recipients: A Scoping Review. *Int. J. Nurs. Pract.* **2025**, *31*, e70010. [CrossRef]
8. Chen, T.H.; Ma, W.F. Exploring Socio-Economic Differences and Developer Medical Involvement of Dementia-Related English Version Mobile Health Applications. *Int. J. Geriatr. Psychiatry* **2025**, *40*, e70064. [CrossRef]
9. Cappadona, I.; Ielo, A.; Pagano, M.; Anselmo, A.; Micali, G.; Giambò, F.M.; Duca, A.; D'Aleo, P.; Costanzo, D.; Carcione, G.; et al. Observational protocol on neuropsychological disorders in cardiovascular disease for holistic prevention and treatment. *Future Cardiol.* **2025**, *21*, 349–358. [CrossRef]
10. Shen, W.C.; Lin, J.N.; Chan, S.H.; Yuh-Shiow, L.; Wang, J.J. Exploring Care Challenges and Needs of People with Diabetes Comorbid Cognitive Impairment from the Triangular Perspectives. *Nurs. Health Sci.* **2025**, *27*, e70081. [CrossRef]
11. Bhalla, G.; Tanoto, P.; Vipin, A.; Chen, X.Y.J.; Leow, Y.J.; Chen, C.; Yap, P.L.K.; Merchant, R.A.; Hilal, S.; Ong, A.P.; et al. Current status and future directions for the diagnosis and management of mild cognitive impairment in Southeast Asia: A SEACURE consensus paper. *J. Prev. Alzheimer's Dis.* **2025**, *12*, 100110. [CrossRef] [PubMed]
12. Doerr, A.J.; Orwig, T.A.; McNulty, M.; Sison, S.D.M.; Paquette, D.R.; Leung, R.; Ding, H.; Erban, S.B.; Weinstein, B.R.; Guilarte-Walker, Y.; et al. Digital Assessment of Cognitive Health in Outpatient Primary Care: Usability Study. *JMIR Form. Res.* **2025**, *9*, e66695. [CrossRef] [PubMed]
13. Yilmaz, B.; Erdogan, C.S.; Sandal, S.; Kelestimur, F.; Carpenter, D.O. Obesogens and Energy Homeostasis: Definition, Mechanisms of Action, Exposure, and Adverse Effects on Human Health. *Neuroendocrinology* **2025**, *115*, 72–100. [CrossRef] [PubMed]
14. Zhukovsky, P.; Tio, E.S.; Coughlan, G.; Bennett, D.A.; Wang, Y.; Hohman, T.J.; Pizzagalli, D.A.; Mulsant, B.H.; Voineskos, A.N.; Felsky, D. Genetic influences on brain and cognitive health and their interactions with cardiovascular conditions and depression. *Nat. Commun.* **2024**, *15*, 5207. [CrossRef]
15. Dudbridge, F.; Pashayan, N.; Yang, J. Predictive accuracy of combined genetic and environmental risk scores. *Genet. Epidemiol.* **2018**, *42*, 4–19. [CrossRef]
16. Willemsen, G.; Vink, J.M.; Abdellaoui, A.; den Braber, A.; van Beek, J.H.D.A.; Draisma, H.H.M.; van Dongen, J.; van 't Ent, D.; Geels, L.M.; van Lien, R.; et al. The Adult Netherlands Twin Register: Twenty-five years of survey and biological data collection. *Twin Res. Hum. Genet. Off. J. Int. Soc. Twin Stud.* **2013**, *16*, 271–281. [CrossRef]
17. Chen, S.; Chen, S.; Hanewald, K.; Si, Y.; Bateman, H.; Li, B.; Xu, X.; Samtani, S.; Wu, C.; Brodaty, H. Social Environment, Lifestyle, and Genetic Predisposition with Dementia Risk: A Long-Term Longitudinal Study Among Older Adults. *J. Gerontol. A. Biol. Sci. Med. Sci.* **2024**, *79*, glae128. [CrossRef]

18. Chermon, D.; Birk, R. Brain-derived neurotrophic factor gene rs925946 associates with Israeli females' obesity predisposition: An interaction between genetics, eating habits, and physical inactivity. *Nutr. Res.* **2024**, *125*, 61–68. [CrossRef]
19. van Dongen, J.; Willemsen, G.; de Geus, E.J.C.; Boomsma, D.I.; Neale, M.C. Effects of smoking on genome-wide DNA methylation profiles: A study of discordant and concordant monozygotic twin pairs. *Elife* **2023**, *12*, e83286. [CrossRef]
20. Pérusse, L.; Jacob, R.; Drapeau, V.; Llewellyn, C.; Arsenault, B.J.; Bureau, A.; Labonté, M.-È.; Tremblay, A.; Vohl, M.-C. Understanding Gene-Lifestyle Interaction in Obesity: The Role of Mediation versus Moderation. *Lifestyle Genom.* **2022**, *15*, 67–76. [CrossRef]
21. Barbu, M.C.; Shen, X.; Walker, R.M.; Howard, D.M.; Evans, K.L.; Whalley, H.C.; Porteous, D.J.; Morris, S.W.; Deary, I.J.; Zeng, Y.; et al. Epigenetic prediction of major depressive disorder. *Mol. Psychiatry* **2021**, *26*, 5112–5123. [CrossRef] [PubMed]
22. Zhou, X.; van der Werf, J.; Carson-Chahhoud, K.; Ni, G.; McGrath, J.; Hyppönen, E.; Lee, S.H. Whole-Genome Approach Discovers Novel Genetic and Nongenetic Variance Components Modulated by Lifestyle for Cardiovascular Health. *J. Am. Heart Assoc.* **2020**, *9*, e015661. [CrossRef] [PubMed]
23. Gibson, J.; Russ, T.C.; Clarke, T.-K.; Howard, D.M.; Hillary, R.F.; Evans, K.L.; Walker, R.M.; Bermingham, M.L.; Morris, S.W.; Campbell, A.; et al. A meta-analysis of genome-wide association studies of epigenetic age acceleration. *PLoS Genet.* **2019**, *15*, e1008104. [CrossRef] [PubMed]
24. Huat, T.J.; Camats-Perna, J.; Newcombe, E.A.; Valmas, N.; Kitazawa, M.; Medeiros, R. Metal Toxicity Links to Alzheimer's Disease and Neuroinflammation. *J. Mol. Biol.* **2019**, *431*, 1843–1868. [CrossRef]
25. Skaper, S.D. The neurotrophin family of neurotrophic factors: An overview. *Methods Mol. Biol.* **2012**, *846*, 1–12. [CrossRef]
26. Numakawa, T.; Kajihara, R. The Role of Brain-Derived Neurotrophic Factor as an Essential Mediator in Neuronal Functions and the Therapeutic Potential of Its Mimetics for Neuroprotection in Neurologic and Psychiatric Disorders. *Molecules* **2025**, *30*, 848. [CrossRef]
27. Carvalho, I.M.; Coelho, P.B.; Costa, P.C.; Marques, C.S.; Oliveira, R.S.; Ferreira, D.C. Current Neurogenic and Neuroprotective Strategies to Prevent and Treat Neurodegenerative and Neuropsychiatric Disorders. *NeuroMolecular Med.* **2015**, *17*, 404–422. [CrossRef]
28. Lewin, G.R. Physiology of the Neurotrophins. *Annu. Rev. Neurosci.* **1996**, *19*, 289–317. [CrossRef]
29. Harvey, T.; Rios, M. The Role of BDNF and TrkB in the Central Control of Energy and Glucose Balance: An Update. *Biomolecules* **2024**, *14*, 424. [CrossRef]
30. Kim, J.; He, M.J.; Widmann, A.K.; Lee, F.S. The role of neurotrophic factors in novel, rapid psychiatric treatments. *Neuropsychopharmacology* **2024**, *49*, 227–245. [CrossRef]
31. Abdolahi, S.; Zare-Chahoki, A.; Noorbakhsh, F.; Gorji, A. A Review of Molecular Interplay between Neurotrophins and miRNAs in Neuropsychological Disorders. *Mol. Neurobiol.* **2022**, *59*, 6260–6280. [CrossRef] [PubMed]
32. Numakawa, T.; Odaka, H. Brain-derived neurotrophic factor signaling in the pathophysiology of alzheimer's disease: Beneficial effects of flavonoids for neuroprotection. *Int. J. Mol. Sci.* **2021**, *22*, 5719. [CrossRef] [PubMed]
33. Lippi, G.; Mattiuzzi, C.; Sanchis-Gomar, F. Updated overview on interplay between physical exercise, neurotrophins, and cognitive function in humans. *J. Sport. Health Sci.* **2020**, *9*, 74–81. [CrossRef] [PubMed]
34. Kashyap, M.P.; Roberts, C.; Waseem, M.; Tyagi, P. Drug Targets in Neurotrophin Signaling in the Central and Peripheral Nervous System. *Mol. Neurobiol.* **2018**, *55*, 6939–6955. [CrossRef]
35. Tang, T.; Li, Y.; Jiao, Q.; Du, X.; Jiang, H. Cerebral Dopamine Neurotrophic Factor: A Potential Therapeutic Agent for Parkinson's Disease. *Neurosci. Bull.* **2017**, *33*, 568–575. [CrossRef]
36. Mitre, M.; Mariga, A.; Chao, M.V. Neurotrophin signalling: Novel insights into mechanisms and pathophysiology. *Clin. Sci.* **2017**, *131*, 13–23. [CrossRef]
37. Ciafrè, S.; Ferraguti, G.; Tirassa, P.; Iannitelli, A.; Ralli, M.; Greco, A.; Chaldakov, G.N.; Rosso, P.; Fico, E.; Messina, M.P.; et al. Nerve growth factor in the psychiatric brain. *Riv. Psichiatr.* **2020**, *55*, 4–15. [CrossRef]
38. Frim, D.M.; Uhler, T.A.; Short, M.P.; Ezzedine, Z.D.; Klagsbrun, M.; Breakefield, X.O.; Isacson, O. Effects of biologically delivered NGF, bdnf and BFGF on striatal excitotoxic lesions. *Neuroreport* **1993**, *4*, 367–370. [CrossRef]
39. Alizadeh Pahlavani, H. Possible role of exercise therapy on depression: Effector neurotransmitters as key players. *Behav. Brain Res.* **2024**, *459*, 114791. [CrossRef]
40. Scuri, M.; Samsell, L.; Piedimonte, G. The role of neurotrophins in inflammation and allergy. *Inflamm. Allergy Drug Targets* **2010**, *9*, 173–180. [CrossRef]
41. Rochlitzer, S.; Nassenstein, C.; Braun, A. The contribution of neurotrophins to the pathogenesis of allergic asthma. *Biochem. Soc. Trans.* **2006**, *34*, 594–599. [CrossRef] [PubMed]
42. Chao, M.Y.; Rajagopal, R.; Lee, F.S. Neurotrophin signalling in health and disease. *Clin. Sci.* **2006**, *110*, 167–173. [CrossRef] [PubMed]
43. Ricci, A.; Felici, L.; Mariotta, S.; Mannino, F.; Schmid, G.; Terzano, C.; Cardillo, G.; Amenta, F.; Bronzetti, E. Neurotrophin and Neurotrophin Receptor Protein Expression in the Human Lung. *Am. J. Respir. Cell Mol. Biol.* **2004**, *30*, 12–19. [CrossRef] [PubMed]

44. Schulte-Herbruggen, O.; Braun, A.; Rochlitzer, S.; Jockers-Scherubl, M.C.; Hellweg, R. Neurotrophic factors--a tool for therapeutic strategies in neurological, neuropsychiatric and neuroimmunological diseases? *Curr. Med. Chem.* **2007**, *14*, 2318–2329. [CrossRef]
45. Angelucci, F.; Mathé, A.A.; Aloe, L. Neurotrophic factors and CNS disorders: Findings in rodent models of depression and schizophrenia. *Prog. Brain Res.* **2004**, *146*, 151–165. [CrossRef]
46. Martinotti, G.; Di Iorio, G.; Marini, S.; Ricci, V.; De Berardis, D.; Di Giannantonio, M. Nerve growth factor and brain-derived neurotrophic factor concentrations in schizophrenia: A review. *J. Biol. Regul. Homeost. Agents* **2012**, *26*, 347–356.
47. Costa, S.L.; Silva, V.D.A.; dos Santos Souza, C.; Santos, C.C.; Paris, I.; Muñoz, P.; Segura-Aguilar, J. Impact of Plant-Derived Flavonoids on Neurodegenerative Diseases. *Neurotox. Res.* **2016**, *30*, 41–52. [CrossRef]
48. Hussain, G.; Huang, J.; Rasul, A.; Anwar, H.; Imran, A.; Maqbool, J.; Razzaq, A.; Aziz, N.; Makhdoom, E.U.H.; Konuk, M.; et al. Putative roles of plant-derived tannins in neurodegenerative and neuropsychiatry disorders: An updated review. *Molecules* **2019**, *24*, 2213. [CrossRef]
49. Mohsenpour, H.; Pesce, M.; Patruno, A.; Bahrami, A.; Pour, P.M.; Farzaei, M.H. A review of plant extracts and plant-derived natural compounds in the prevention/treatment of neonatal hypoxic-ischemic brain injury. *Int. J. Mol. Sci.* **2021**, *22*, 833. [CrossRef]
50. Fakhri, S.; Abbaszadeh, F.; Moradi, S.Z.; Cao, H.; Khan, H.; Xiao, J. Effects of Polyphenols on Oxidative Stress, Inflammation, and Interconnected Pathways during Spinal Cord Injury. *Oxidative Med. Cell. Longev.* **2022**, *2022*, 8100195. [CrossRef]
51. Tayab, M.A.; Islam, M.N.; Chowdhury, K.A.A.; Tasnim, F.M. Targeting neuroinflammation by polyphenols: A promising therapeutic approach against inflammation-associated depression. *Biomed. Pharmacother.* **2022**, *147*, 112668. [CrossRef]
52. Davinelli, S.; Medoro, A.; Ali, S.; Passarella, D.; Intrieri, M.; Scapagnini, G. Dietary Flavonoids and Adult Neurogenesis: Potential Implications for Brain Aging. *Curr. Neuropharmacol.* **2022**, *21*, 651–668. [CrossRef] [PubMed]
53. Shi, R.; Gao, D.; Stoika, R.; Liu, K.; Sik, A.; Jin, M. Potential implications of polyphenolic compounds in neurodegenerative diseases. *Crit. Rev. Food Sci. Nutr.* **2024**, *64*, 5491–5514. [CrossRef] [PubMed]
54. Grabska-Kobyłecka, I.; Szpakowski, P.; Król, A.; Książek-Winiarek, D.; Kobyłecki, A.; Głąbiński, A.; Nowak, D. Polyphenols and Their Impact on the Prevention of Neurodegenerative Diseases and Development. *Nutrients* **2023**, *15*, 3454. [CrossRef]
55. Roy, D.; Kaur, P.; Ghosh, M.; Choudhary, D.; Rangra, N.K. The therapeutic potential of typical plant-derived compounds for the management of metabolic disorders. *Phyther. Res.* **2024**, *38*, 3986–4008. [CrossRef] [PubMed]
56. Moise, G.; Jîjie, A.R.; Moacă, E.A.; Predescu, I.A.; Dehelean, C.A.; Heghes, A.; Vlad, D.C.; Popescu, R.; Vlad, C.S. Plants' Impact on the Human Brain—Exploring the Neuroprotective and Neurotoxic Potential of Plants. *Pharmaceuticals* **2024**, *17*, 1339. [CrossRef]
57. Miguel, C.A.; Noya-Riobó, M.V.; Mazzone, G.L.; Villar, M.J.; Coronel, M.F. Antioxidant, anti-inflammatory and neuroprotective actions of resveratrol after experimental nervous system insults. Special focus on the molecular mechanisms involved. *Neurochem. Int.* **2021**, *150*, 105188. [CrossRef]
58. Goyal, S.; Seth, B.; Chaturvedi, R.K. Polyphenols and Stem Cells for Neuroregeneration in Parkinson's Disease and Amyotrophic Lateral Sclerosis. *Curr. Pharm. Des.* **2021**, *28*, 806–828. [CrossRef]
59. Özduran, G.; Becer, E.; Vatansever, H.S. The Role and Mechanisms of Action of Catechins in Neurodegenerative Diseases. *J. Am. Nutr. Assoc.* **2023**, *42*, 67–74. [CrossRef]
60. Alesci, A.; Nicosia, N.; Fumia, A.; Giorgianni, F.; Santini, A.; Cicero, N. Resveratrol and Immune Cells: A Link to Improve Human Health. *Molecules* **2022**, *27*, 424. [CrossRef]
61. Nor, N.A.M.; Budin, S.B.; Zainalabidin, S.; Jalil, J.; Sapian, S.; Jubaidi, F.F.; Anuar, N.N.M. The Role of Polyphenol in Modulating Associated Genes in Diabetes-Induced Vascular Disorders. *Int. J. Mol. Sci.* **2022**, *23*, 6396. [CrossRef]
62. Zhang, W.; Dong, X.; Huang, R. Antiparkinsonian effects of polyphenols: A narrative review with a focus on the modulation of the gut-brain axis. *Pharmacol. Res.* **2023**, *193*, 106787. [CrossRef] [PubMed]
63. Bhusal, C.K.; Uti, D.E.; Mukherjee, D.; Alqahtani, T.; Alqahtani, S.; Bhattacharya, A.; Akash, S. Unveiling Nature's potential: Promising natural compounds in Parkinson's disease management. *Park. Relat. Disord.* **2023**, *115*, 105799. [CrossRef] [PubMed]
64. Gong, G.; Ganesan, K.; Wan, Y.; Liu, Y.; Huang, Y.; Luo, Y.; Wang, X.; Zhang, Z.; Zheng, Y. Unveiling the neuroprotective properties of isoflavones: Current evidence, molecular mechanisms and future perspectives. *Crit. Rev. Food Sci. Nutr.* **2024**, *65*, 3112–3148. [CrossRef]
65. Carito, V.; Ceccanti, M.; Tarani, L.; Ferraguti, G.; NChaldakov, G.; Fiore, M. Neurotrophins' Modulation by Olive Polyphenols. *Curr. Med. Chem.* **2016**, *23*, 3189–3197. [CrossRef]
66. Carito, V.; Ceccanti, M.; Ferraguti, G.; Coccurello, R.; Ciafrè, S.; Tirassa, P.; Fiore, M. NGF and BDNF Alterations by Prenatal Alcohol Exposure. *Curr. Neuropharmacol.* **2019**, *17*, 308–317. [CrossRef]
67. Tarani, L.; Carito, V.; Ferraguti, G.; Petrella, C.; Greco, A.; Ralli, M.; Messina, M.P.; Rasio, D.; De Luca, E.; Putotto, C.; et al. Neuroinflammatory Markers in the Serum of Prepubertal Children with down Syndrome. *J. Immunol. Res.* **2020**, *2020*, 6937154. [CrossRef]

68. Ferraguti, G.; Terracina, S.; Tarani, L.; Fanfarillo, F.; Allushi, S.; Caronti, B.; Tirassa, P.; Polimeni, A.; Lucarelli, M.; Cavalcanti, L.; et al. Nerve Growth Factor and the Role of Inflammation in Tumor Development. *Curr. Issues Mol. Biol.* **2024**, *46*, 965–989. [CrossRef]
69. Pardon, M.C. Role of Neurotrophic Factors in Behavioral Processes: Implications for the Treatment of Psychiatric and Neurodegenerative Disorders. *Vitam. Horm.* **2010**, *82*, 185–200. [CrossRef]
70. Fujii, T.; Kunugi, H. p75NTR as a Therapeutic Target for Neuropsychiatric Diseases. *Curr. Mol. Pharmacol.* **2010**, *2*, 70–76. [CrossRef]
71. Retamales-Ortega, R.; Oróstica, L.; Vera, C.; Cuevas, P.; Hernández, A.; Hurtado, I.; Vega, M.; Romero, C. Role of nerve growth factor (NGF) and miRNAs in epithelial ovarian cancer. *Int. J. Mol. Sci.* **2017**, *18*, 507. [CrossRef] [PubMed]
72. Meeker, R.B.; Williams, K.S. The p75 neurotrophin receptor: At the crossroad of neural repair and death. *Neural Regen. Res.* **2015**, *10*, 721–725. [CrossRef] [PubMed]
73. Kozlov, E.M.; Grechko, A.V.; Chegodaev, Y.S.; Wu, W.K.; Orekhov, A.N. Contribution of neurotrophins to the immune system regulation and possible connection to alcohol addiction. *Biology* **2020**, *9*, 63. [CrossRef]
74. West, A.E.; Pruunsild, P.; Timmusk, T. Neurotrophins: Transcription and translation. *Handb. Exp. Pharmacol.* **2014**, *220*, 67–100. [CrossRef] [PubMed]
75. Tonchev, A.B. Brain ischemia, neurogenesis, and neurotrophic receptor expression in primates. *Arch. Ital. Biol.* **2011**, *149*, 225–231. [CrossRef]
76. Cirulli, F.; Alleva, E. The NGF saga: From animal models of psychosocial stress to stress-related psychopathology. *Front. Neuroendocrinol.* **2009**, *30*, 379–395. [CrossRef]
77. Fields, J.; Dumaop, W.; Langford, T.D.; Rockenstein, E.; Masliah, E. Role of neurotrophic factor alterations in the neurodegenerative process in HIV associated neurocognitive disorders. *J. Neuroimmune Pharmacol.* **2014**, *9*, 102–116. [CrossRef]
78. Von Bartheld, C.S. Neurotrophins in the developing and regenerating visual system. *Histol. Histopathol.* **1998**, *13*, 437–459.
79. Huang, E.J.; Reichardt, L.F. Trk Receptors: Roles in Neuronal Signal Transduction. *Annu. Rev. Biochem.* **2003**, *72*, 609–642. [CrossRef]
80. Leßmann, V. Neurotrophin-dependent modulation of glutamatergic synaptic transmission in the mammalian CNS. *Gen. Pharmacol.* **1998**, *31*, 667–674. [CrossRef]
81. Meis, S.; Endres, T.; Lessmann, V. Neurotrophin signalling in amygdala-dependent cued fear learning. *Cell Tissue Res.* **2020**, *382*, 161–172. [CrossRef] [PubMed]
82. Fernandez, G.M.; Stewart, W.N.; Savage, L.M. Chronic drinking during adolescence predisposes the adult rat for continued heavy drinking: Neurotrophin and behavioral adaptation after long-term, continuous ethanol exposure. *PLoS ONE* **2016**, *11*, e0149987. [CrossRef] [PubMed]
83. Aloe, L.; Iannitelli, A.; Angelucci, F.; Bersani, G.; Fiore, M. Studies in animal models and humans suggesting a role of nerve growth factor in schizophrenia-like disorders. *Behav. Pharmacol.* **2000**, *11*, 235–242. [CrossRef] [PubMed]
84. Bersani, G.; Iannitelli, A.; Fiore, M.; Angelucci, F.; Aloe, L. Data and hypotheses on the role of nerve growth factor and other neurotrophins in psychiatric disorders. *Med. Hypotheses* **2000**, *55*, 199–207. [CrossRef]
85. Aloe, L.; Rocco, M.L.; Bianchi, P.; Manni, L. Nerve growth factor: From the early discoveries to the potential clinical use. *J. Transl. Med.* **2012**, *10*, 239. [CrossRef]
86. Dechant, G.; Neumann, H. Neurotrophins. *Adv. Exp. Med. Biol.* **2002**, *513*, 303–334. [CrossRef]
87. Longo, F.M.; Massa, S.M. Neurotrophin-based strategies for neuroprotection. *J. Alzheimers Dis.* **2004**, *6*, S13–S17. [CrossRef]
88. Fiore, M.; Amendola, T.; Triaca, V.; Tirassa, P.; Alleva, E.; Aloe, L. Agonistic encounters in aged male mouse potentiate the expression of endogenous brain NGF and BDNF: Possible implication for brain progenitor cells' activation. *Eur. J. Neurosci.* **2003**, *17*, 1455–1464. [CrossRef]
89. Mooney, S.M.; Miller, M.W. Nerve growth factor neuroprotection of ethanol-induced neuronal death in rat cerebral cortex is age dependent. *Neuroscience* **2007**, *149*, 372–381. [CrossRef]
90. Ebadi, M.; Bashir, R.M.; Heidrick, M.L.; Hamada, F.M.; Refaey, H.E.L.; Hamed, A.; Helal, G.; Baxi, M.D.; Cerutis, D.R.; Lassi, N.K. Neurotrophins and their receptors in nerve injury and repair. *Neurochem. Int.* **1997**, *30*, 347–374. [CrossRef]
91. Ichim, G.; Tauszig-Delamasure, S.; Mehlen, P. Neurotrophins and cell death. *Exp. Cell Res.* **2012**, *318*, 1221–1228. [CrossRef] [PubMed]
92. Meakin, S.O.; Shooter, E.M. The nerve growth factor family of receptors. *Trends Neurosci.* **1992**, *15*, 323–331. [CrossRef] [PubMed]
93. Chen, E.; Mufson, E.J.; Kordower, J.H. TRK and p75 Neurotrophin Receptor Systems in the Developing Human Brain. *J. Comp. Neurol.* **1996**, *618*, 591–618. [CrossRef]
94. Cacialli, P. Neurotrophins time point intervention after traumatic brain injury: From zebrafish to human. *Int. J. Mol. Sci.* **2021**, *22*, 1585. [CrossRef]
95. Nakagawara, A. Trk receptor tyrosine kinases: A bridge between cancer and neural development. *Cancer Lett.* **2001**, *169*, 107–114. [CrossRef]

96. Reichardt, L.F. Neurotrophin-regulated signalling pathways. *Philos. Trans. R. Soc. B Biol. Sci.* **2006**, *361*, 1545–1564. [CrossRef]
97. French, S.J.; Humby, T.; Horner, C.H.; Sofroniew, M.V.; Rattray, M. Hippocampal neurotrophin and trk receptor mRNA levels are altered by local administration of nicotine, carbachol and pilocarpine. *Mol. Brain Res.* **1999**, *67*, 124–136. [CrossRef]
98. Molloy, N.H.; Read, D.E.; Gorman, A.M. Nerve growth factor in cancer cell death and survival. *Cancers* **2011**, *3*, 510–530. [CrossRef]
99. Nguyen, N.; Lee, S.B.; Lee, Y.S.; Lee, K.H.; Ahn, J.Y. Neuroprotection by NGF and BDNF against neurotoxin-exerted apoptotic death in neural stem cells are mediated through Trk receptors, activating PI3-kinase and MAPK pathways. *Neurochem. Res.* **2009**, *34*, 942–951. [CrossRef]
100. Braunger, B.M.; Demmer, C.; Tamm, E.R. Programmed cell death during retinal development of the mouse eye. *Adv. Exp. Med. Biol.* **2014**, *801*, 9–13. [CrossRef]
101. Chakravarthy, R.; Mnich, K.; Gorman, A.M. Nerve growth factor (NGF)-mediated regulation of p75NTR expression contributes to chemotherapeutic resistance in triple negative breast cancer cells. *Biochem. Biophys. Res. Commun.* **2016**, *478*, 1541–1547. [CrossRef] [PubMed]
102. Yan, C.; Liang, Y.; Nylander, K.D.; Wong, J.; Rudavsky, R.M.; Saragovi, H.U.; Schor, N.F. p75-nerve growth factor as an antiapoptotic complex: Independence versus cooperativity in protection from enediyne chemotherapeutic agents. *Mol. Pharmacol.* **2002**, *61*, 710–719. [CrossRef] [PubMed]
103. Lu, B.; Pang, P.T.; Woo, N.H. The yin and yang of neurotrophin action. *Nat. Rev. Neurosci.* **2005**, *6*, 603–614. [CrossRef] [PubMed]
104. Björkholm, C.; Monteggia, L.M. BDNF—A key transducer of antidepressant effects. *Neuropharmacology* **2016**, *102*, 72–79. [CrossRef]
105. Ryu, S.; Liu, X.; Guo, T.; Guo, Z.; Zhang, J.; Cao, Y.Q. Peripheral CCL2-CCR2 signalling contributes to chronic headache-related sensitization. *Brain* **2023**, *146*, 4274–4291. [CrossRef]
106. Zhang, H.L.; Sun, Y.; Wu, Z.J.; Yin, Y.; Liu, R.Y.; Zhang, J.C.; Zhang, Z.J.; Yau, S.Y.; Wu, H.X.; Yuan, T.F.; et al. Hippocampal PACAP signaling activation triggers a rapid antidepressant response. *Mil. Med. Res.* **2024**, *11*, 49. [CrossRef]
107. Contreras, E.; Bolívar, S.; Navarro, X.; Udina, E. New insights into peripheral nerve regeneration: The role of secretomes. *Exp. Neurol.* **2022**, *354*, 114069. [CrossRef]
108. Osborne, A.; Khatib, T.Z.; Songra, L.; Barber, A.C.; Hall, K.; Kong, G.Y.X.; Widdowson, P.S.; Martin, K.R. Neuroprotection of retinal ganglion cells by a novel gene therapy construct that achieves sustained enhancement of brain-derived neurotrophic factor/tropomyosin-related kinase receptor-B signaling. *Cell Death Dis.* **2018**, *9*, 1007. [CrossRef]
109. Peplow, P.V.; Baxter, G.D. Gene expression and release of growth factors during delayed wound healing: A review of studies in diabetic animals and possible combined laser phototherapy and growth factor treatment to enhance healing. *Photomed. Laser Surg.* **2012**, *30*, 617–636. [CrossRef]
110. Hou, C.H.; Chen, W.L.; Lin, C.Y. Targeting nerve growth factor-mediated osteosarcoma metastasis: Mechanistic insights and therapeutic opportunities using larotrectinib. *Cell Death Dis.* **2024**, *15*, 381. [CrossRef]
111. Manni, L.; Aloe, L.; Fiore, M. Changes in cognition induced by social isolation in the mouse are restored by electro-acupuncture. *Physiol. Behav.* **2009**, *98*, 537–542. [CrossRef] [PubMed]
112. Wei, K.; Yang, J.; Lin, S.; Mei, Y.; An, N.; Cao, X.; Jiang, L.; Liu, C.; Li, C. Dietary Habits Modify the Association of Physical Exercise with Cognitive Impairment in Community-Dwelling Older Adults. *J. Clin. Med.* **2022**, *11*, 5122. [CrossRef] [PubMed]
113. Barati, S.; Fabrizio, C.; Strafella, C.; Cascella, R.; Caputo, V.; Megalizzi, D.; Peconi, C.; Mela, J.; Colantoni, L.; Caltagirone, C.; et al. Relationship between Nutrition, Lifestyle, and Neurodegenerative Disease: Lessons from ADH1B, CYP1A2 and MTHFR. *Genes* **2022**, *13*, 1498. [CrossRef] [PubMed]
114. Faurot, K.R.; Cole, W.R.; MacIntosh, B.A.; Dunlap, M.; Moore, C.B.; Roberson, B.; Guerra, M.; Domenichiello, A.F.; Palsson, O.; Rivera, W.; et al. Targeted dietary interventions to reduce pain in persistent post-traumatic headache among service members: Protocol for a randomized, controlled parallel-group trial. *Contemp. Clin. Trials* **2022**, *119*, 106851. [CrossRef]
115. Driver, S.; McShan, E.; Swank, C.; Grobe, K.; Calhoun, S.; Bailey, R.; Kramer, K. Creating an appropriate adaptation of a healthy lifestyle intervention for people after stroke. *Brain Inj.* **2020**, *34*, 1497–1503. [CrossRef]
116. Durany, N.; Thome, J. Neurotrophic factors and the pathophysiology of schizophrenic psychoses. *Eur. Psychiatry* **2004**, *19*, 326–337. [CrossRef]
117. Jiang, C.; Salton, S.R. The role of neurotrophins in major depressive disorder. *Transl. Neurosci.* **2013**, *4*, 46–58. [CrossRef]
118. Fukuyama, Y.; Kubo, M.; Harada, K. The search for, and chemistry and mechanism of, neurotrophic natural products. *J. Nat. Med.* **2020**, *74*, 648–671. [CrossRef]
119. Memberg, S.P.; Hall, A.K. Proliferation, differentiation, and survival of rat sensory neuron precursors in vitro require specific trophic factors. *Mol. Cell. Neurosci.* **1995**, *6*, 323–335. [CrossRef]
120. Alvarez-Dolado, M.; Iglesias, T.; Rodríguez-Peña, A.; Bernal, J.; Muñoz, A. Expression of neurotrophins and the trk family of neurotrophin receptors in normal and hypothyroid rat brain. *Mol. Brain Res.* **1994**, *27*, 249–257. [CrossRef]
121. Fiore, M.; Grace, A.A.; Korf, J.; Stampachiacchiere, B.; Aloe, L. Impaired brain development in the rat following prenatal exposure to methylazoxymethanol acetate at gestational day 17 and neurotrophin distribution. *Neuroreport* **2004**, *15*, 1791–1795. [CrossRef]

122. Valvassori, S.S.; Mariot, E.; Varela, R.B.; Bavaresco, D.V.; Dal-Pont, G.C.; Ferreira, C.L.; Andersen, M.L.; Tye, S.J.; Quevedo, J. The role of neurotrophic factors in manic-, anxious- and depressive-like behaviors induced by amphetamine sensitization: Implications to the animal model of bipolar disorder. *J. Affect. Disord.* **2019**, *245*, 1106–1113. [CrossRef] [PubMed]
123. Ceccanti, M.; Mancinelli, R.; Tirassa, P.; Laviola, G.; Rossi, S.; Romeo, M.; Fiore, M. Early exposure to ethanol or red wine and long-lasting effects in aged mice. A study on nerve growth factor, brain-derived neurotrophic factor, hepatocyte growth factor, and vascular endothelial growth factor. *Neurobiol. Aging* **2012**, *33*, 359–367. [CrossRef] [PubMed]
124. Van der Zee, C.E.E.M.; Rashid, K.; Le, K.; Moore, K.A.; Stanisz, J.; Diamond, J.; Racine, R.J.; Fahnestock, M. Intraventricular administration of antibodies to nerve growth factor retards kindling and blocks mossy fiber sprouting in adult rats. *J. Neurosci.* **1995**, *15*, 5316–5323. [CrossRef] [PubMed]
125. Angelucci, F.; Mathé, A.A.; Aloe, L. Brain-derived neurotrophic factor and tyrosine kinase receptor TrkB in rat brain are significantly altered after haloperidol and risperidone administration. *J. Neurosci. Res.* **2000**, *60*, 783–794. [CrossRef]
126. Bimonte-Nelson, H.A.; Hunter, C.L.; Nelson, M.E.; Granholm, A.C. Frontal cortex BDNF levels correlate with working memory in an animal model of Down syndrome. *Behav. Brain Res.* **2003**, *139*, 47–57. [CrossRef]
127. Ferraguti, G.; Terracina, S.; Micangeli, G.; Lucarelli, M.; Tarani, L.; Ceccanti, M.; Spaziani, M.; D'Orazi, V.; Petrella, C.; Fiore, M. NGF and BDNF in pediatrics syndromes. *Neurosci. Biobehav. Rev.* **2023**, *145*, 105015. [CrossRef]
128. Ciafrè, S.; Ferraguti, G.; Greco, A.; Polimeni, A.; Ralli, M.; Ceci, F.M.; Ceccanti, M.; Fiore, M. Alcohol as an early life stressor: Epigenetics, metabolic, neuroendocrine and neurobehavioral implications. *Neurosci. Biobehav. Rev.* **2020**, *118*, 654–668. [CrossRef]
129. Manni, L.; Fausto, V.; Fiore, M.; Aloe, L. Repeated Restraint and Nerve Growth Factor Administration in Male and Female Mice: Effect on Sympathetic and Cardiovascular Mediators of the Stress Response. *Curr. Neurovasc. Res.* **2008**, *5*, 1–12. [CrossRef]
130. Aloe, L.; Alleva, E.; Fiore, M. Stress and nerve growth factor: Findings in animal models and humans. *Pharmacol. Biochem. Behav.* **2002**, *73*, 159–166. [CrossRef]
131. Ceci, F.M.; Ferraguti, G.; Petrella, C.; Greco, A.; Tirassa, P.; Iannitelli, A.; Ralli, M.; Vitali, M.; Ceccanti, M.; Chaldakov, G.N.; et al. Nerve Growth Factor, Stress and Diseases. *Curr. Med. Chem.* **2020**, *28*, 2943–2959. [CrossRef] [PubMed]
132. Di Liegro, C.M.; Schiera, G.; Proia, P.; Di Liegro, I. Physical activity and brain health. *Genes* **2019**, *10*, 720. [CrossRef] [PubMed]
133. Sanaeifar, F.; Pourranjbar, S.; Pourranjbar, M.; Ramezani, S.; Mehr, S.R.; Wadan, A.H.S.; Khazeifard, F. Beneficial effects of physical exercise on cognitive-behavioral impairments and brain-derived neurotrophic factor alteration in the limbic system induced by neurodegeneration. *Exp. Gerontol.* **2024**, *195*, 112539. [CrossRef] [PubMed]
134. Almeida, M.F.; Chaves, R.S.; Silva, C.M.; Chaves, J.C.S.; Melo, K.P.; Ferrari, M.F.R. BDNF trafficking and signaling impairment during early neurodegeneration is prevented by moderate physical activity. *IBRO Rep.* **2016**, *1*, 19–31. [CrossRef]
135. Fiore, M.; Talamini, L.; Angelucci, F.; Koch, T.; Aloe, L.; Korf, J. Prenatal methylazoxymethanol acetate alters behavior and brain NGF levels in young rats: A possible correlation with the development of schizophrenia-like deficits. *Neuropharmacology* **1999**, *38*, 857–869. [CrossRef]
136. Weinstock, M. Prenatal stressors in rodents: Effects on behavior. *Neurobiol. Stress* **2017**, *6*, 3–13. [CrossRef]
137. De Nicoló, S.; Tarani, L.; Ceccanti, M.; Maldini, M.; Natella, F.; Vania, A.; Chaldakov, G.N.; Fiore, M. Effects of olive polyphenols administration on nerve growth factor and brain-derived neurotrophic factor in the mouse brain. *Nutrition* **2013**, *29*, 681–687. [CrossRef]
138. Moosavi, F.; Hosseini, R.; Saso, L.; Firuzi, O. Modulation of neurotrophic signaling pathways by polyphenols. *Drug Des. Devel. Ther.* **2015**, *10*, 23–42. [CrossRef]
139. Ziegler, T.; Tsiountsioura, M.; Meixner-Goetz, L.; Cvirn, G.; Lamprecht, M. Polyphenols' Impact on Selected Biomarkers of Brain Aging in Healthy Middle-Aged and Elderly Subjects: A Review of Clinical Trials. *Nutrients* **2023**, *15*, 3770. [CrossRef]
140. Kopalli, S.R.; Behl, T.; Kyada, A.; Rekha, M.M.; Kundlas, M.; Rani, P.; Nathiya, D.; Satyam Naidu, K.; Gulati, M.; Bhise, M.; et al. Synaptic plasticity and neuroprotection: The molecular impact of flavonoids on neurodegenerative disease progression. *Neuroscience* **2025**, *569*, 161–183. [CrossRef]
141. An, J.; Chen, B.; Tian, D.; Guo, Y.; Yan, Y.; Yang, H. Regulation of Neurogenesis and Neuronal Differentiation by Natural Compounds. *Curr. Stem Cell Res. Ther.* **2022**, *17*, 756–771. [CrossRef] [PubMed]
142. Nicoletti, V.G.; Pajer, K.; Calcagno, D.; Pajenda, G.; Nógrádi, A. The Role of Metals in the Neuroregenerative Action of BDNF, GDNF, NGF and Other Neurotrophic Factors. *Biomolecules* **2022**, *12*, 1015. [CrossRef] [PubMed]
143. Mitra, S.; Behbahani, H.; Eriksdotter, M. Innovative therapy for Alzheimer's disease-with focus on biodelivery of NGF. *Front. Neurosci.* **2019**, *13*, 38. [CrossRef] [PubMed]
144. Stepanichev, M.; Onufriev, M.; Aniol, V.; Freiman, S.; Brandstaetter, H.; Winter, S.; Lazareva, N.; Guekht, A.; Gulyaeva, N. Effects of cerebrolysin on nerve growth factor system in the aging rat brain. *Restor. Neurol. Neurosci.* **2017**, *35*, 571–581. [CrossRef]
145. Forlenza, O.V.; Miranda, A.S.; Barbosa, I.G.; Talib, L.L.; Diniz, B.S.; Gattaz, W.F.; Teixeira, A.L. Decreased neurotrophic support is associated with cognitive decline in non-demented subjects. *J. Alzheimer's Dis.* **2015**, *46*, 423–429. [CrossRef]
146. Sable, P.; Kale, A.; Joshi, A.; Joshi, S. Maternal micronutrient imbalance alters gene expression of BDNF, NGF, TrkB and CREB in the offspring brain at an adult age. *Int. J. Dev. Neurosci. Off. J. Int. Soc. Dev. Neurosci.* **2014**, *34*, 24–32. [CrossRef]

147. Riccio, A.; Ahn, S.; Davenport, C.M.; Blendy, J.A.; Ginty, D.D. Mediation by a CREB family transcription factor of NGF-dependent survival of sympathetic neurons. *Science* **1999**, *286*, 2358–2361. [CrossRef]
148. Cheng, A.; Hou, Y.; Mattson, M.P. Mitochondria and neuroplasticity. *ASN Neuro* **2010**, *2*, e00045. [CrossRef]
149. Almeida, S.; Cunha-Oliveira, T.; Laço, M.; Oliveira, C.R.; Rego, A.C. Dysregulation of CREB activation and histone acetylation in 3-nitropropionic acid-treated cortical neurons: Prevention by BDNF and NGF. *Neurotox. Res.* **2010**, *17*, 399–405. [CrossRef]
150. Fiore, M.; Petrella, C.; Coriale, G.; Rosso, P.; Fico, E.; Ralli, M.; Greco, A.; De Vincentiis, M.; Minni, A.; Polimeni, A.; et al. Markers of Neuroinflammation in the Serum of Prepubertal Children with Fetal Alcohol Spectrum Disorders. *CNS Neurol. Disord. Drug Targets-CNS Neurol. Disord.* **2022**, *21*, 854–868. [CrossRef]
151. Pahlavani, H.A. Exercise therapy to prevent and treat Alzheimer's disease. *Front. Aging Neurosci.* **2023**, *15*, 1243869. [CrossRef] [PubMed]
152. Gong, A.G.W.; Wang, H.Y.; Dong, T.T.X.; Tsim, K.W.K.; Zheng, Y.Z. Danggui Buxue Tang, a simple Chinese formula containing Astragali Radix and Angelicae Sinensis Radix, stimulates the expressions of neurotrophic factors in cultured SH-SY5Y cells. *Chin. Med.* **2017**, *12*, 24. [CrossRef] [PubMed]
153. Primiani, C.T.; Ryan, V.H.; Rao, J.S.; Cam, M.C.; Ahn, K.; Modi, H.R.; Rapoport, S.I. Coordinated gene expression of neuroinflammatory and cell signaling markers in dorsolateral prefrontal cortex during human brain development and aging. *PLoS ONE* **2014**, *9*, e110972. [CrossRef]
154. Griñán-Ferré, C.; Marsal-García, L.; Bellver-Sanchis, A.; Kondengaden, S.M.; Turga, R.C.; Vázquez, S.; Pallàs, M. Pharmacological inhibition of G9a/GLP restores cognition and reduces oxidative stress, neuroinflammation and ß-Amyloid plaques in an early-onset Alzheimer's disease mouse model. *Aging* **2019**, *11*, 11591–11608. [CrossRef]
155. Liu, J.; Wang, Y.; Guo, J.; Sun, J.; Sun, Q. Salvianolic Acid B improves cognitive impairment by inhibiting neuroinflammation and decreasing Aß level in Porphyromonas gingivalis-infected mice. *Aging* **2020**, *12*, 10117–10128. [CrossRef] [PubMed]
156. Sun, Y.; Shi, X.; Ohm, M.; Korte, M.; Zagrebelsky, M. Deciphering genetic causality between plasma BDNF and 91 circulating inflammatory proteins through bidirectional mendelian randomization. *Sci. Rep.* **2025**, *15*, 10312. [CrossRef]
157. Braschi, C.; Capsoni, S.; Narducci, R.; Poli, A.; Sansevero, G.; Brandi, R.; Maffei, L.; Cattaneo, A.; Berardi, N. Intranasal delivery of BDNF rescues memory deficits in AD11 mice and reduces brain microgliosis. *Aging Clin. Exp. Res.* **2021**, *33*, 1223–1238. [CrossRef]
158. Wang, Z.H.; Xiang, J.; Liu, X.; Yu, S.P.; Manfredsson, F.P.; Sandoval, I.M.; Wu, S.; Wang, J.Z.; Ye, K. Deficiency in BDNF/TrkB Neurotrophic Activity Stimulates δ-Secretase by Upregulating C/EBPβ in Alzheimer's Disease. *Cell Rep.* **2019**, *28*, 655–669.e5. [CrossRef]
159. Wu, C.C.; Lien, C.C.; Hou, W.H.; Chiang, P.M.; Tsai, K.J. Gain of BDNF Function in Engrafted Neural Stem Cells Promotes the Therapeutic Potential for Alzheimer's Disease. *Sci. Rep.* **2016**, *6*, 27358. [CrossRef]
160. Turnbull, M.T.; Boskovic, Z.; Coulson, E.J. Acute down-regulation of BDNF signaling does not replicate exacerbated amyloid-β levels and cognitive impairment induced by cholinergic basal forebrain lesion. *Front. Mol. Neurosci.* **2018**, *11*, 51. [CrossRef]
161. Xu, J.; Kurup, P.; Azkona, G.; Baguley, T.D.; Saavedra, A.; Nairn, A.C.; Ellman, J.A.; Pérez-Navarro, E.; Lombroso, P.J. Down-regulation of BDNF in cell and animal models increases striatal-enriched protein tyrosine phosphatase 61 (STEP61) levels. *J. Neurochem.* **2016**, *136*, 285–294. [CrossRef] [PubMed]
162. Velazquez, R.; Ferreira, E.; Tran, A.; Turner, E.C.; Belfiore, R.; Branca, C.; Oddo, S. Acute tau knockdown in the hippocampus of adult mice causes learning and memory deficits. *Aging Cell* **2018**, *17*, e12775. [CrossRef] [PubMed]
163. Sartor, G.C.; Malvezzi, A.M.; Kumar, A.; Andrade, N.S.; Wiedner, H.J.; Vilca, S.J.; Janczura, K.J.; Bagheri, A.; Al-Ali, H.; Powell, S.K.; et al. Enhancement of BDNF expression and memory by HDAC inhibition requires BET bromodomain reader proteins. *J. Neurosci.* **2019**, *39*, 612–626. [CrossRef] [PubMed]
164. Zhu, G.; Sun, X.; Yang, Y.; Du, Y.; Lin, Y.; Zhou, N.; Xiang, J. Reduction of BDNF Results in GABAergic Neuroplasticity Dysfunction and Contributes to Late-Life Anxiety Disorder. *Behav. Neurosci.* **2019**, *133*, 212–224. [CrossRef]
165. Wang, L.; Mao, Y.; Lu, Y.; Yuan, Y.; Jin, Y. Knockdown of lncRNA BDNF-AS alleviates isoflurane-induced neuro-inflammation and cognitive dysfunction through modulating miR-214-3p. *Folia Neuropathol.* **2023**, *61*, 68–76. [CrossRef]
166. Carrillo, J.Á.; Arcusa, R.; Xandri-Martínez, R.; Cerdá, B.; Zafrilla, P.; Marhuenda, J. Impact of Polyphenol-Rich Nutraceuticals on Cognitive Function and Neuroprotective Biomarkers: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *Nutrients* **2025**, *17*, 601. [CrossRef]
167. Puhlmann, L.M.C.; Vrtička, P.; Linz, R.; Valk, S.L.; Papassotiriou, I.; Chrousos, G.P.; Engert, V.; Singer, T. Serum BDNF Increase After 9-Month Contemplative Mental Training Is Associated with Decreased Cortisol Secretion and Increased Dentate Gyrus Volume: Evidence from a Randomized Clinical Trial. *Biol. Psychiatry Glob. Open Sci.* **2025**, *5*, 100414. [CrossRef]
168. Kim, N.; Parolin, B.; Renshaw, D.; Deb, S.K.; Zariwala, M.G. Formulated Palmitoylethanolamide Supplementation Improves Parameters of Cognitive Function and BDNF Levels in Young, Healthy Adults: A Randomised Cross-Over Trial. *Nutrients* **2024**, *16*, 489. [CrossRef]

169. Schneider, E.; Doll, J.P.K.; Schweinfurth, N.; Kettelhack, C.; Schaub, A.C.; Yamanbaeva, G.; Varghese, N.; Mählmann, L.; Brand, S.; Eckert, A.; et al. Effect of short-term, high-dose probiotic supplementation on cognition, related brain functions and BDNF in patients with depression: A secondary analysis of a randomized controlled trial. *J. Psychiatry Neurosci.* **2023**, *48*, E23–E33. [CrossRef]
170. Hsu, Y.C.; Huang, Y.Y.; Tsai, S.Y.; Kuo, Y.W.; Lin, J.H.; Ho, H.H.; Chen, J.F.; Hsia, K.C.; Sun, Y. Efficacy of Probiotic Supplements on Brain-Derived Neurotrophic Factor, Inflammatory Biomarkers, Oxidative Stress and Cognitive Function in Patients with Alzheimer's Dementia: A 12-Week Randomized, Double-Blind Active-Controlled Study. *Nutrients* **2024**, *16*, 16. [CrossRef]
171. Tsao, R. Chemistry and biochemistry of dietary polyphenols. *Nutrients* **2010**, *2*, 1231–1246. [CrossRef] [PubMed]
172. Wan, M.L.Y.; Co, V.A.; El-Nezami, H. Dietary polyphenol impact on gut health and microbiota. *Crit. Rev. Food Sci. Nutr.* **2021**, *61*, 690–711. [CrossRef] [PubMed]
173. Shen, N.; Wang, T.; Gan, Q.; Liu, S.; Wang, L.; Jin, B. Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. *Food Chem.* **2022**, *383*, 132531. [CrossRef] [PubMed]
174. Iqbal, I.; Wilairatana, P.; Saqib, F.; Nasir, B.; Wahid, M.; Latif, M.F.; Iqbal, A.; Naz, R.; Mubarak, M.S. Plant Polyphenols and Their Potential Benefits on Cardiovascular Health: A Review. *Molecules* **2023**, *28*, 6403. [CrossRef]
175. Luca, S.V.; Macovei, I.; Bujor, A.; Miron, A.; Skalicka-Woźniak, K.; Aprotosoaie, A.C.; Trifan, A. Bioactivity of dietary polyphenols: The role of metabolites. *Crit. Rev. Food Sci. Nutr.* **2020**, *60*, 626–659. [CrossRef]
176. Rana, A.; Samtiya, M.; Dhewa, T.; Mishra, V.; Aluko, R.E. Health benefits of polyphenols: A concise review. *J. Food Biochem.* **2022**, *46*, e14264. [CrossRef]
177. Truzzi, F.; Tibaldi, C.; Zhang, Y.; Dinelli, G.; DAmen, E. An Overview on Dietary Polyphenols and Their Biopharmaceutical Classification System (BCS). *Int. J. Mol. Sci.* **2021**, *22*, 5514. [CrossRef]
178. Zhang, L.; Han, Z.; Granato, D. Polyphenols in foods: Classification, methods of identification, and nutritional aspects in human health. *Adv. Food Nutr. Res.* **2021**, *98*, 1–33. [CrossRef]
179. Ciupei, D.; Colişar, A.; Leopold, L.; Stănilă, A.; Diaconeasa, Z.M. Polyphenols: From Classification to Therapeutic Potential and Bioavailability. *Foods* **2024**, *13*, 4131. [CrossRef]
180. Chong, J.R.; de Lucia, C.; Tovar-Rios, D.A.; Castellanos-Perilla, N.; Collins, C.; Kvernberg, S.M.; Ballard, C.; Siow, R.C.; Aarsland, D. A Randomised, Double-Blind, Placebo-Controlled, Cross-Over Clinical Trial to Evaluate the Biological Effects and Safety of a Polyphenol Supplement on Healthy Ageing. *Antioxidants* **2024**, *13*, 995. [CrossRef]
181. Godos, J.; Caraci, F.; Castellano, S.; Currenti, W.; Galvano, F.; Ferri, R.; Grosso, G. Association between dietary flavonoids intake and cognitive function in an Italian cohort. *Biomolecules* **2020**, *10*, 1300. [CrossRef] [PubMed]
182. Gorzynik-Debicka, M.; Przychodzen, P.; Cappello, F.; Kuban-Jankowska, A.; Gammazza, A.M.; Knap, N.; Wozniak, M.; Gorska-Ponikowska, M. Potential health benefits of olive oil and plant polyphenols. *Int. J. Mol. Sci.* **2018**, *19*, 686. [CrossRef] [PubMed]
183. Abd El-Hack, M.E.; de Oliveira, M.C.; Attia, Y.A.; Kamal, M.; Almohmadi, N.H.; Youssef, I.M.; Khalifa, N.E.; Moustafa, M.; Al-Shehri, M.; Taha, A.E. The efficacy of polyphenols as an antioxidant agent: An updated review. *Int. J. Biol. Macromol.* **2023**, *250*, 126525. [CrossRef]
184. Zhou, Y.; Zhang, S.; Fan, X. Role of Polyphenols as Antioxidant Supplementation in Ischemic Stroke. *Oxid. Med. Cell. Longev.* **2021**, *2021*, 5471347. [CrossRef] [PubMed]
185. Panickar, K.S.; Anderson, R.A. Effect of polyphenols on oxidative stress and mitochondrial dysfunction in neuronal death and brain edema in cerebral ischemia. *Int. J. Mol. Sci.* **2011**, *12*, 8181–8207. [CrossRef]
186. Zhou, Z.D.; Xie, S.P.; Saw, W.T.; Ho, P.G.H.; Wang, H.; Lei, Z.; Yi, Z.; Tan, E.K. The therapeutic implications of tea polyphenols against dopamine (DA) neuron degeneration in parkinson's disease (PD). *Cells* **2019**, *8*, 911. [CrossRef]
187. Cracco, P.; Montalesi, E.; Parente, M.; Cipolletti, M.; Iucci, G.; Battocchio, C.; Venditti, I.; Fiocchetti, M.; Marino, M. A Novel Resveratrol-Induced Pathway Increases Neuron-Derived Cell Resilience against Oxidative Stress. *Int. J. Mol. Sci.* **2023**, *24*, 5903. [CrossRef]
188. Kung, H.C.; Lin, K.J.; Kung, C.T.; Lin, T.K. Oxidative stress, mitochondrial dysfunction, and neuroprotection of polyphenols with respect to resveratrol in parkinson's disease. *Biomedicines* **2021**, *9*, 918. [CrossRef]
189. Naoi, M.; Wu, Y.; Shamoto-Nagai, M.; Maruyama, W. Mitochondria in Neuroprotection by Phytochemicals: Bioactive Polyphenols Modulate Mitochondrial Apoptosis System, Function and Structure. *Int. J. Mol. Sci.* **2019**, *20*, 2451. [CrossRef]
190. Zhou, Y.; Jiang, Z.; Lu, H.; Xu, Z.; Tong, R.; Shi, J.; Jia, G. Recent Advances of Natural Polyphenols Activators for Keap1-Nrf2 Signaling Pathway. *Chem. Biodivers.* **2019**, *16*, e1900400. [CrossRef]
191. Nabavi, S.F.; Barber, A.J.; Spagnuolo, C.; Russo, G.L.; Daglia, M.; Nabavi, S.M.; Sobarzo-Sánchez, E. Nrf2 as molecular target for polyphenols: A novel therapeutic strategy in diabetic retinopathy. *Crit. Rev. Clin. Lab. Sci.* **2016**, *53*, 293–312. [CrossRef] [PubMed]
192. Tascioglu Aliyev, A.; Panieri, E.; Stepanić, V.; Gurer-Orhan, H.; Saso, L. Involvement of NRF2 in Breast Cancer and Possible Therapeutical Role of Polyphenols and Melatonin. *Molecules* **2021**, *26*, 1853. [CrossRef] [PubMed]

193. Plauth, A.; Geikowski, A.; Cichon, S.; Wowro, S.J.; Liedgens, L.; Rousseau, M.; Weidner, C.; Fuhr, L.; Kliem, M.; Jenkins, G.; et al. Hormetic shifting of redox environment by pro-oxidative resveratrol protects cells against stress. *Free Radic. Biol. Med.* **2016**, *99*, 608–622. [CrossRef] [PubMed]
194. Figueira, I.; Menezes, R.; Macedo, D.; Costa, I.; dos Santos, C.N. Polyphenols Beyond Barriers: A Glimpse into the Brain. *Curr. Neuropharmacol.* **2016**, *15*, 562–594. [CrossRef]
195. Gundimeda, U.; McNeill, T.H.; Schiffman, J.E.; Hinton, D.R.; Gopalakrishna, R. Green tea polyphenols potentiate the action of nerve growth factor to induce neuritogenesis: Possible role of reactive oxygen species. *J. Neurosci. Res.* **2010**, *88*, 3644–3655. [CrossRef]
196. Bensalem, J.; Dudonne, S.; Gaudout, D.; Servant, L.; Calon, F.; Desjardins, Y.; Laye, S.; Lafenetre, P.; Pallet, V. Polyphenol-rich extract from grape and blueberry attenuates cognitive decline and improves neuronal function in aged mice. *J. Nutr. Sci.* **2018**, *7*, e19. [CrossRef]
197. Fiore, M.; Messina, M.P.; Petrella, C.; D'Angelo, A.; Greco, A.; Ralli, M.; Ferraguti, G.; Tarani, L.; Vitali, M.; Ceccanti, M. Antioxidant properties of plant polyphenols in the counteraction of alcohol-abuse induced damage: Impact on the Mediterranean diet. *J. Funct. Foods* **2020**, *71*, 104012. [CrossRef]
198. Bucio-Noble, D.; Kautto, L.; Krisp, C.; Ball, M.S.; Molloy, M.P. Polyphenol extracts from dried sugarcane inhibit inflammatory mediators in an in vitro colon cancer model. *J. Proteom.* **2018**, *177*, 1–10. [CrossRef]
199. Pallauf, K.; Giller, K.; Huebbe, P.; Rimbach, G. Nutrition and healthy ageing: Calorie restriction or polyphenol-rich "mediterrAsian" diet? *Oxidative Med. Cell. Longev.* **2013**, *2013*, 707421. [CrossRef]
200. Ajmo, J.M.; Liang, X.; Rogers, C.Q.; Pennock, B.; You, M. Resveratrol alleviates alcoholic fatty liver in mice. *AJP Gastrointest. Liver Physiol.* **2008**, *295*, G833–G842. [CrossRef]
201. Han, S.; Choi, J.R.; Soon Shin, K.; Kang, S.J. Resveratrol upregulated heat shock proteins and extended the survival of G93A-SOD1 mice. *Brain Res.* **2012**, *1483*, 112–117. [CrossRef] [PubMed]
202. El Hayek, L.; Khalifeh, M.; Zibara, V.; Abi Assaad, R.; Emmanuel, N.; Karnib, N.; El-Ghandour, R.; Nasrallah, P.; Bilen, M.; Ibrahim, P.; et al. Lactate mediates the effects of exercise on learning and memory through sirt1-dependent activation of hippocampal brain-derived neurotrophic factor (BDNF). *J. Neurosci.* **2019**, *39*, 2369–2382. [CrossRef] [PubMed]
203. Wu, W.F.; Chen, C.; Lin, J.T.; Jiao, X.H.; Dong, W.; Wan, J.; Liu, Q.; Qiu, Y.K.; Sun, A.; Liu, Y.Q.; et al. Impaired synaptic plasticity and decreased glutamatergic neuron excitability induced by SIRT1/BDNF downregulation in the hippocampal CA1 region are involved in postoperative cognitive dysfunction. *Cell. Mol. Biol. Lett.* **2024**, *29*, 79. [CrossRef]
204. Caruso, G.I.; Spampinato, S.F.; Costantino, G.; Merlo, S.; Sortino, M.A. SIRT1-dependent upregulation of BDNF in human microglia challenged with Aβ: An early but transient response rescued by melatonin. *Biomedicines* **2021**, *9*, 466. [CrossRef] [PubMed]
205. Liu, M.; Li, C.; Li, R.; Yin, D.; Hong, Y.; Lu, M.; Xia, B.; Li, Y. Resveratrol by elevating the SIRT1 BDNF, GDNF and PSD95 levels reduce heroin addiction related behaviors. *Neurosci. Lett.* **2024**, *841*, 137934. [CrossRef]
206. Wang, F.; Li, Y.; Tang, D.; Yang, B.; Tian, T.; Tian, M.; Meng, N.; Xie, W.; Zhang, C.; He, Z.; et al. Exploration of the SIRT1-mediated BDNF–TrkB signaling pathway in the mechanism of brain damage and learning and memory effects of fluorosis. *Front. Public Heal.* **2023**, *11*, 1247294. [CrossRef]
207. Zhang, L.; Fang, Y.; Xu, Y.; Lian, Y.; Xie, N.; Wu, T.; Zhang, H.; Sun, L.; Zhang, R.; Wang, Z. Curcumin improves amyloid β-peptide (1-42) induced spatial memory deficits through BDNF-ERK signaling pathway. *PLoS ONE* **2015**, *10*, e0131525. [CrossRef]
208. Goozee, K.G.; Shah, T.M.; Sohrabi, H.R.; Rainey-Smith, S.R.; Brown, B.; Verdile, G.; Martins, R.N. Examining the potential clinical value of curcumin in the prevention and diagnosis of Alzheimer's disease. *Br. J. Nutr.* **2016**, *115*, 449–465. [CrossRef]
209. Lou, S.; Gong, D.; Yang, M.; Qiu, Q.; Luo, J.; Chen, T. Curcumin Improves Neurogenesis in Alzheimer's Disease Mice via the Upregulation of Wnt/β-Catenin and BDNF. *Int. J. Mol. Sci.* **2024**, *25*, 5123. [CrossRef]
210. Pervin, M.; Unno, K.; Ohishi, T.; Tanabe, H.; Miyoshi, N.; Nakamura, Y. Beneficial Effects of Green Tea Catechins on Neurodegenerative Diseases. *Molecules* **2018**, *23*, 1297. [CrossRef]
211. Zhang, S.; Zhu, Q.; Chen, J.Y.; OuYang, D.; Lu, J.H. The pharmacological activity of epigallocatechin-3-gallate (EGCG) on Alzheimer's disease animal model: A systematic review. *Phytomedicine* **2020**, *79*, 153316. [CrossRef] [PubMed]
212. Sharma, R.; Bhate, L.; Agrawal, Y.; Aspatwar, A. Advanced nutraceutical approaches to Parkinson's disease: Bridging nutrition and neuroprotection. *Nutr. Neurosci.* **2025**, 1–17. [CrossRef] [PubMed]
213. Valverde-Salazar, V.; Ruiz-Gabarre, D.; García-Escudero, V. Alzheimer's Disease and Green Tea: Epigallocatechin-3-Gallate as a Modulator of Inflammation and Oxidative Stress. *Antioxidants* **2023**, *12*, 1460. [CrossRef] [PubMed]
214. Sebastiani, G.; Almeida-Toledano, L.; Serra-Delgado, M.; Navarro-Tapia, E.; Sailer, S.; Valverde, O.; Garcia-Algar, O.; Andreu-Fernández, V. Therapeutic effects of catechins in less common neurological and neurodegenerative disorders. *Nutrients* **2021**, *13*, 2232. [CrossRef]

215. Xu, Y.; Xie, M.; Xue, J.; Xiang, L.; Li, Y.; Xiao, J.; Xiao, G.; Wang, H.L. EGCG ameliorates neuronal and behavioral defects by remodeling gut microbiota and TotM expression in Drosophila models of Parkinson's disease. *FASEB J.* **2020**, *34*, 5931–5950. [CrossRef]
216. Shi, W.; Li, L.; Ding, Y.; Yang, K.; Chen, Z.; Fan, X.; Jiang, S.; Guan, Y.; Liu, Z.; Xu, D.; et al. The critical role of epigallocatechin gallate in regulating mitochondrial metabolism. *Future Med. Chem.* **2018**, *10*, 795–809. [CrossRef]
217. de Oliveira, M.R.; Nabavi, S.F.; Daglia, M.; Rastrelli, L.; Nabavi, S.M. Epigallocatechin gallate and mitochondria—A story of life and death. *Pharmacol. Res.* **2016**, *104*, 70–85. [CrossRef]
218. Ayyalasomayajula, N.; Bandaru, L.J.M.; Chetty, C.S.; Dixit, P.K.; Challa, S. Mitochondria-Mediated Moderation of Apoptosis by EGCG in Cytotoxic Neuronal Cells Induced by Lead (Pb) and Amyloid Peptides. *Biol. Trace Elem. Res.* **2022**, *200*, 3582–3593. [CrossRef]
219. Tseng, H.L.; Li, C.J.; Huang, L.H.; Chen, C.Y.; Tsai, C.H.; Lin, C.N.; Hsu, H.Y. Quercetin 3-O-methyl ether protects FL83B cells from copper induced oxidative stress through the PI3K/Akt and MAPK/Erk pathway. *Toxicol. Appl. Pharmacol.* **2012**, *264*, 104–113. [CrossRef]
220. Safi, A.; Heidarian, E.; Ahmadi, R. Quercetin Synergistically Enhances the Anticancer Efficacy of Docetaxel through Induction of Apoptosis and Modulation of PI3K/AKT, MAPK/ERK, and JAK/STAT3 Signaling Pathways in MDA-MB-231 Breast Cancer Cell Line. *Int. J. Mol. Cell. Med.* **2021**, *10*, 11. [CrossRef]
221. Terracina, S.; Petrella, C.; Francati, S.; Lucarelli, M.; Barbato, C.; Minni, A.; Ralli, M.; Greco, A.; Tarani, L.; Fiore, M.; et al. Antioxidant Intervention to Improve Cognition in the Aging Brain: The Example of Hydroxytyrosol and Resveratrol. *Int. J. Mol. Sci.* **2022**, *23*, 15674. [CrossRef] [PubMed]
222. Boronat, A.; Serreli, G.; Rodríguez-Morató, J.; Deiana, M.; de la Torre, R. Olive Oil Phenolic Compounds' Activity against Age-Associated Cognitive Decline: Clinical and Experimental Evidence. *Antioxidants* **2023**, *12*, 1472. [CrossRef] [PubMed]
223. Casamenti, F.; Stefani, M. Olive polyphenols: New promising agents to combat aging-associated neurodegeneration. *Expert Rev. Neurother.* **2017**, *17*, 345–358. [CrossRef] [PubMed]
224. Micheli, L.; Bertini, L.; Bonato, A.; Villanova, N.; Caruso, C.; Caruso, M.; Bernini, R.; Tirone, F. Role of Hydroxytyrosol and Oleuropein in the Prevention of Aging and Related Disorders: Focus on Neurodegeneration, Skeletal Muscle Dysfunction and Gut Microbiota. *Nutrients* **2023**, *15*, 1767. [CrossRef]
225. Mititelu, M.; Lupuliasa, D.; Neacșu, S.M.; Olteanu, G.; Busnatu, Ș.S.; Mihai, A.; Popovici, V.; Măru, N.; Boroghină, S.C.; Mihai, S.; et al. Polyunsaturated Fatty Acids and Human Health: A Key to Modern Nutritional Balance in Association with Polyphenolic Compounds from Food Sources. *Foods* **2025**, *14*, 46. [CrossRef]
226. Vidyanti, A.N.; Rahmawati, F.; Rahman, R.H.; Prodjohardjono, A.; Gofir, A. Lifestyle interventions for dementia risk reduction: A review on the role of physical activity and diet in Western and Asian Countries. *J. Prev. Alzheimer's Dis.* **2025**, *12*, 100028. [CrossRef]
227. Stefani, M.; Rigacci, S. Beneficial properties of natural phenols: Highlight on protection against pathological conditions associated with amyloid aggregation. *BioFactors* **2014**, *40*, 482–493. [CrossRef]
228. Kozioł-Kozakowska, A.; Wójcik, M.; Herceg-Čavrak, V.; Cobal, S.; Radovanovic, D.; Alvarez-Pitti, J.; Hartgring, I.; Piórecka, B.; Gabbianelli, R.; Drożdż, D. Dietary Strategies in the Prevention and Treatment of Hypertension in Children and Adolescents: A Narrative Review. *Nutrients* **2024**, *16*, 2786. [CrossRef]
229. Sudarshan, K.; Boda, A.K.; Dogra, S.; Bose, I.; Yadav, P.N.; Aidhen, I.S. Discovery of an isocoumarin analogue that modulates neuronal functions via neurotrophin receptor TrkB. *Bioorganic Med. Chem. Lett.* **2019**, *29*, 585–590. [CrossRef]
230. Román, G.C.; Jackson, R.E.; Gadhia, R.; Román, A.N.; Reis, J. Mediterranean diet: The role of long-chain ω-3 fatty acids in fish; polyphenols in fruits, vegetables, cereals, coffee, tea, cacao and wine; probiotics and vitamins in prevention of stroke, age-related cognitive decline, and Alzheimer disease. *Rev. Neurol.* **2019**, *175*, 724–741. [CrossRef]
231. Canudas, S.; Becerra-Tomas, N.; Hernandez-Alonso, P.; Galie, S.; Leung, C.; Crous-Bou, M.; De Vivo, I.; Gao, Y.; Gu, Y.; Meinila, J.; et al. Mediterranean Diet and Telomere Length: A Systematic Review and Meta-Analysis. *Adv. Nutr.* **2020**, *11*, 1544–1554. [CrossRef] [PubMed]
232. van Soest, A.P.; Beers, S.; van de Rest, O.; de Groot, L.C. The Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) Diet for the Aging Brain: A Systematic Review. *Adv. Nutr.* **2024**, *15*, 100184. [CrossRef] [PubMed]
233. McGrattan, A.M.; McGuinness, B.; McKinley, M.C.; Kee, F.; Passmore, P.; Woodside, J.V.; McEvoy, C.T. Diet and Inflammation in Cognitive Ageing and Alzheimer's Disease. *Curr. Nutr. Rep.* **2019**, *8*, 53–65. [CrossRef] [PubMed]
234. Morris, M.C.; Tangney, C.C.; Wang, Y.; Sacks, F.M.; Barnes, L.L.; Bennett, D.A.; Aggarwal, N.T. MIND diet slows cognitive decline with aging. *Alzheimer's Dement.* **2015**, *11*, 1015–1022. [CrossRef]
235. Stefaniak, O.; Dobrzyńska, M.; Drzymała-Czyż, S.; Przysławski, J. Diet in the Prevention of Alzheimer's Disease: Current Knowledge and Future Research Requirements. *Nutrients* **2022**, *14*, 4564. [CrossRef]

236. Valls-Pedret, C.; Lamuela-Raventós, R.M.; Medina-Remón, A.; Quintana, M.; Corella, D.; Pintó, X.; Martínez-González, M.Á.; Estruch, R.; Ros, E. Polyphenol-rich foods in the mediterranean diet are associated with better cognitive function in elderly subjects at high cardiovascular risk. *J. Alzheimer's Dis.* **2012**, *29*, 773–782. [CrossRef]
237. Lopresti, A.L.; Smith, S.J.; Pouchieu, C.; Pourtau, L.; Gaudout, D.; Pallet, V.; Drummond, P.D. Effects of a polyphenol-rich grape and blueberry extract (Memophenol^{TM}) on cognitive function in older adults with mild cognitive impairment: A randomized, double-blind, placebo-controlled study. *Front. Psychol.* **2023**, *14*, 1144231. [CrossRef]
238. Sasaki, A.; Kawai, E.; Watanabe, K.; Yamano, E.; Oba, C.; Nakamura, K.; Natsume, M.; Mizuno, K.; Watanabe, Y. Cacao Polyphenol-Rich Dark Chocolate Intake Contributes to Efficient Brain Activity during Cognitive Tasks: A Randomized, Single-Blinded, Crossover, and Dose-Comparison fMRI Study. *Nutrients* **2024**, *16*, 41. [CrossRef]
239. Rajaram, S.; Jones, J.; Lee, G.J. Plant-based dietary patterns, plant foods, and age-related cognitive decline. *Adv. Nutr.* **2019**, *10*, 422–436. [CrossRef]
240. Riegelman, E.; Xue, K.S.; Wang, J.S.; Tang, L. Gut–Brain Axis in Focus: Polyphenols, Microbiota, and Their Influence on α-Synuclein in Parkinson's Disease. *Nutrients* **2024**, *16*, 2041. [CrossRef]
241. Sarubbo, F.; Moranta, D.; Tejada, S.; Jiménez, M.; Esteban, S. Impact of Gut Microbiota in Brain Ageing: Polyphenols as Beneficial Modulators. *Antioxidants* **2023**, *12*, 812. [CrossRef] [PubMed]
242. Prakash Reddy, V.; Aryal, P.; Robinson, S.; Rafiu, R.; Obrenovich, M.; Perry, G. Polyphenols in alzheimer's disease and in the gut–brain axis. *Microorganisms* **2020**, *8*, 199. [CrossRef]
243. Filosa, S.; Di Meo, F.; Crispi, S. Polyphenols-gut microbiota interplay and brain neuromodulation. *Neural Regen. Res.* **2018**, *13*, 2055–2059. [CrossRef] [PubMed]
244. Kurhaluk, N.; Kamiński, P.; Bilski, R.; Kołodziejska, R.; Woźniak, A.; Tkaczenko, H. Role of Antioxidants in Modulating the Microbiota–Gut–Brain Axis and Their Impact on Neurodegenerative Diseases. *Int. J. Mol. Sci.* **2025**, *26*, 3658. [CrossRef]
245. Tahiri, M.; Gilbert, J.A. Examining the potential prebiotic effect of almonds. *J. Appl. Microbiol.* **2025**, *136*, lxaf078. [CrossRef]
246. Domínguez-López, I.; López-Yerena, A.; Vallverdú-Queralt, A.; Pallàs, M.; Lamuela-Raventós, R.M.; Pérez, M. From the gut to the brain: The long journey of phenolic compounds with neurocognitive effects. *Nutr. Rev.* **2024**, *83*, e533–e546. [CrossRef]
247. Cao, Q.; Shen, M.; Li, R.; Liu, Y.; Zeng, Z.; Zhou, J.; Niu, D.; Zhang, Q.; Wang, R.; Yao, J.; et al. Elucidating the specific mechanisms of the gut-brain axis: The short-chain fatty acids-microglia pathway. *J. Neuroinflammation* **2025**, *22*, 133. [CrossRef]
248. Molska, M.; Mruczyk, K.; Cisek-Woźniak, A.; Prokopowicz, W.; Szydełko, P.; Jakuszewska, Z.; Marzec, K.; Trocholepsza, M. The Influence of Intestinal Microbiota on BDNF Levels. *Nutrients* **2024**, *16*, 2891. [CrossRef]
249. Arora, I.; Sharma, M.; Sun, L.Y.; Tollefsbol, T.O. The epigenetic link between polyphenols, aging and age-related diseases. *Genes* **2020**, *11*, 1094. [CrossRef]
250. Pan, M.-H.; Lai, C.-S.; Wu, J.-C.; Ho, C.-T. Epigenetic and Disease Targets by Polyphenols. *Curr. Pharm. Des.* **2013**, *19*, 6156–6185. [CrossRef]
251. Prasanth, M.I.; Sivamaruthi, B.S.; Cheong, C.S.Y.; Verma, K.; Tencomnao, T.; Brimson, J.M.; Prasansuklab, A. Role of Epigenetic Modulation in Neurodegenerative Diseases: Implications of Phytochemical Interventions. *Antioxidants* **2024**, *13*, 606. [CrossRef] [PubMed]
252. Borsoi, F.T.; Neri-Numa, I.A.; de Oliveira, W.Q.; de Araújo, F.F.; Pastore, G.M. Dietary polyphenols and their relationship to the modulation of non-communicable chronic diseases and epigenetic mechanisms: A mini-review. *Food Chem. Mol. Sci.* **2023**, *6*, 100155. [CrossRef] [PubMed]
253. Branco, C.S.; Duong, A.; Machado, A.K.; Scola, G.; Andreazza, A.C.; Salvador, M. Modulation of Mitochondrial and Epigenetic Targets by Polyphenols-rich Extract from Araucaria angustifolia in Larynx Carcinoma. *Anticancer Agents Med. Chem.* **2018**, *19*, 130–139. [CrossRef] [PubMed]
254. Cuevas, A.; Saavedra, N.; Salazar, L.A.; Abdalla, D.S.P. Modulation of immune function by polyphenols: Possible contribution of epigenetic factors. *Nutrients* **2013**, *5*, 2314–2332. [CrossRef]
255. Bankole, O.; Scambi, I.; Parrella, E.; Muccilli, M.; Bonafede, R.; Turano, E.; Pizzi, M.; Mariotti, R. Beneficial and Dimorphic Response to Combined HDAC Inhibitor Valproate and AMPK/SIRT1 Pathway Activator Resveratrol in the Treatment of ALS Mice. *Int. J. Mol. Sci.* **2022**, *23*, 1047. [CrossRef]
256. Schiaffino, L.; Bonafede, R.; Scambi, I.; Parrella, E.; Pizzi, M.; Mariotti, R. Acetylation state of RelA modulated by epigenetic drugs prolongs survival and induces a neuroprotective effect on ALS murine model. *Sci. Rep.* **2018**, *8*, 12875. [CrossRef]
257. Zhu, X.; Li, Q.; Chang, R.; Yang, D.; Song, Z.; Guo, Q.; Huang, C. Curcumin alleviates neuropathic pain by inhibiting p300/CBP histone acetyltransferase activity-regulated expression of BDNF and Cox-2 in a rat model. *PLoS ONE* **2014**, *9*, e91303. [CrossRef]
258. Liang, D.Y.; Li, X.; Clark, J.D. Epigenetic regulation of opioid-induced hyperalgesia, dependence, and tolerance in mice. *J. Pain* **2013**, *14*, 36–47. [CrossRef]
259. Lim, U.; Song, M.A. Dietary and lifestyle factors of DNA methylation. *Methods Mol. Biol.* **2012**, *863*, 359–376. [CrossRef]
260. Ribarič, S. Diet and aging. *Oxid. Med. Cell. Longev.* **2012**, *2012*, 741468. [CrossRef]

261. Divyajanani, S.; Harithpriya, K.; Ganesan, K.; Ramkumar, K.M. Dietary Polyphenols Remodel DNA Methylation Patterns of NRF2 in Chronic Disease. *Nutrients* **2023**, *15*, 3347. [CrossRef] [PubMed]
262. Ramalingam, M.; Kim, S.J. Pharmacological activities and applications of spicatoside A. *Biomol. Ther.* **2016**, *24*, 469–474. [CrossRef] [PubMed]
263. Minichiello, L.; Calella, A.M.; Medina, D.L.; Bonhoeffer, T.; Klein, R.; Korte, M. Mechanism of TrkB-mediated hippocampal long-term potentiation. *Neuron* **2002**, *36*, 121–137. [CrossRef] [PubMed]
264. Fiorentino, H.; Kuczewski, N.; Diabira, D.; Ferrand, N.; Pangalos, M.N.; Porcher, C.; Gaiarsa, J.-L. GABAB Receptor Activation Triggers BDNF Release and Promotes the Maturation of GABAergic Synapses. *J. Neurosci.* **2009**, *29*, 11650–11661. [CrossRef]
265. Chen, L.; Zhang, H.Y. Cancer preventive mechanisms of the green tea polyphenol (-)-epigallocatechin-3-gallate. *Molecules* **2007**, *12*, 946–957. [CrossRef]
266. Singh, M.; Arseneault, M.; Sanderson, T.; Murthy, V.; Ramassamy, C. Challenges for research on polyphenols from foods in Alzheimer's disease: Bioavailability, metabolism, and cellular and molecular mechanisms. *J. Agric. Food Chem.* **2008**, *56*, 4855–4873. [CrossRef]
267. Piroddi, M.; Albini, A.; Fabiani, R.; Giovannelli, L.; Luceri, C.; Natella, F.; Rosignoli, P.; Rossi, T.; Taticchi, A.; Servili, M.; et al. Nutrigenomics of extra-virgin olive oil: A review. *BioFactors* **2017**, *43*, 17–41. [CrossRef]
268. Strasser, B.; Gostner, J.M.; Fuchs, D. Mood, food, and cognition: Role of tryptophan and serotonin. *Curr. Opin. Clin. Nutr. Metab. Care* **2016**, *19*, 55–61. [CrossRef]
269. Li, Y.R.; Li, S.; Lin, C.C. Effect of resveratrol and pterostilbene on aging and longevity. *BioFactors* **2018**, *44*, 69–82. [CrossRef]
270. Weinreb, O.; Mandel, S.; Amit, T.; Youdim, M.B. Neurological mechanisms of green tea polyphenols in Alzheimer's and Parkinson's diseases. *J. Nutr. Biochem.* **2004**, *15*, 506–516. [CrossRef]
271. Gandhi, G.R.; Antony, P.J.; de Paula Lana, M.J.M.; da Silva, B.F.X.; Oliveira, R.V.; Jothi, G.; Hariharan, G.; Mohana, T.; Gan, R.Y.; Gurgel, R.Q.; et al. Natural products modulating interleukins and other inflammatory mediators in tumor-bearing animals: A systematic review. *Phytomedicine* **2022**, *100*, 154038. [CrossRef] [PubMed]
272. Cao, S.; Fu, X.; Yang, S.; Tang, S. The anti-inflammatory activity of resveratrol in acute kidney injury: A systematic review and meta-analysis of animal studies. *Pharm. Biol.* **2022**, *60*, 2088–2097. [CrossRef] [PubMed]
273. Jomova, K.; Alomar, S.Y.; Valko, R.; Liska, J.; Nepovimova, E.; Kuca, K.; Valko, M. Flavonoids and their role in oxidative stress, inflammation, and human diseases. *Chem. Biol. Interact.* **2025**, *413*, 111489. [CrossRef] [PubMed]
274. Tiwari, V.; Chopra, K. Resveratrol abrogates alcohol-induced cognitive deficits by attenuating oxidative-nitrosative stress and inflammatory cascade in the adult rat brain. *Neurochem. Int.* **2013**, *62*, 861–869. [CrossRef]
275. Tiwari, V.; Chopra, K. Resveratrol prevents alcohol-induced cognitive deficits and brain damage by blocking inflammatory signaling and cell death cascade in neonatal rat brain. *J. Neurochem.* **2011**, *117*, 678–690. [CrossRef]
276. Kita, T.; Asanuma, M.; Miyazaki, I.; Takeshima, M. Protective Effects of Phytochemical Antioxidants Against Neurotoxin-Induced Degeneration of Dopaminergic Neurons. *J. Pharmacol. Sci.* **2014**, *124*, 313–319. [CrossRef]
277. Chandler, D.; Woldu, A.; Rahmadi, A.; Shanmugam, K.; Steiner, N.; Wright, E.; Benavente-García, O.; Schulz, O.; Castillo, J.; Münch, G. Effects of plant-derived polyphenols on TNF-alpha and nitric oxide production induced by advanced glycation endproducts. *Mol. Nutr. Food Res.* **2010**, *54*, S141–S150. [CrossRef]
278. Asadi, S.; Ahmadiani, A.; Esmaeili, M.A.; Sonboli, A.; Ansari, N.; Khodagholi, F. In vitro antioxidant activities and an investigation of neuroprotection by six Salvia species from Iran: A comparative study. *Food Chem. Toxicol.* **2010**, *48*, 1341–1349. [CrossRef]
279. Goutham, G.; Manikandan, R.; Arulvasu, C.; Arumugam, M.; Beulaja, M.; Thiagarajan, R.; Setzer, W.N.; Daglia, M.; Nabavi, S.F.; Nabavi, S.M. A focus on resveratrol and ocular problems, especially cataract: From chemistry to medical uses and clinical relevance. *Biomed. Pharmacother.* **2017**, *86*, 232–241. [CrossRef]
280. Yahfoufi, N.; Alsadi, N.; Jambi, M.; Matar, C. The immunomodulatory and anti-inflammatory role of polyphenols. *Nutrients* **2018**, *10*, 1618. [CrossRef]
281. Edgecombe, S.C.; Stretch, G.L.; Hayball, P.J. Oleuropein, an antioxidant polyphenol from olive oil, is poorly absorbed from isolated perfused rat intestine. *J. Nutr.* **2000**, *130*, 2996–3002. [CrossRef] [PubMed]
282. Segovia-Bravo, K.A.; Arroyo-Lopez, F.N.; Garcia-Garcia, P.; Duran-Quintana, M.C.; Garrido-Fernandez, A. Reuse of ozonated alkaline solutions as fermentation brines in Spanish green table olives. *J. Food Sci.* **2007**, *72*, M126–M133. [CrossRef] [PubMed]
283. Li, L.; Wang, Z.; Yu, Z.; Niu, T. Dietary Flavonoid Intake and Anemia Risk in Children and Adolescents: Insights from National Health and Nutrition Examination Survey. *Antioxidants* **2025**, *14*, 395. [CrossRef] [PubMed]
284. Amidfar, M.; Garcez, M.L.; Askari, G.; Bagherniya, M.; Khorvash, F.; Golpour-Hamedani, S.; de Oliveira, J. Role of BDNF Signaling in the Neuroprotective and Memory-enhancing Effects of Flavonoids in Alzheimer's Disease. *CNS Neurol. Disord. Drug Targets* **2024**, *23*, 984–995. [CrossRef]
285. Melgar-Locatelli, S.; Mañas-Padilla, M.C.; Castro-Zavala, A.; Rivera, P.; del Carmen Razola-Díaz, M.; Monje, F.J.; Rodríguez-Pérez, C.; Castilla-Ortega, E. Diet enriched with high-phenolic cocoa potentiates hippocampal brain-derived neurotrophic factor expression and neurogenesis in healthy adult micewith subtle effects on memory. *Food Funct.* **2024**, *15*, 8310–8329. [CrossRef]

286. Tan, L.; Zhang, H.; Li, H.; Sun, S.; Lyu, Q.; Jiang, Y. Blueberry extracts antagonize Aβ25–35 neurotoxicity and exert a neuroprotective effect through MEK-ERK-BDNF/UCH-L1 signaling pathway in rat and mouse hippocampus. *Nutr. Neurosci.* **2024**, *27*, 745–760. [CrossRef]
287. Babaei, F.G.; Saburi, E.; Forouzanfar, F.; Asgari, M.; Keshavarzi, Z.; Hajali, V. Effect of epigallocatechin-3-gallate (EGCG) on cognitive functioning and the expression of APP and BDNF in the hippocampus of rats with streptozotocin -induced Alzheimer-like disease. *Biochem. Biophys. Rep.* **2025**, *41*, 101930. [CrossRef]
288. Hammad, A.M.; Alzaghari, L.F.; Alfaraj, M.; Lux, V.; Sunoqrot, S. Green Tea Polyphenol Nanoparticles Reduce Anxiety Caused by Tobacco Smoking Withdrawal in Rats by Suppressing Neuroinflammation. *Toxics* **2024**, *12*, 598. [CrossRef]
289. Jalouli, M.; Rahman, M.A.; Biswas, P.; Rahman, H.; Harrath, A.H.; Lee, I.S.; Kang, S.; Choi, J.; Park, M.N.; Kim, B. Targeting natural antioxidant polyphenols to protect neuroinflammation and neurodegenerative diseases: A comprehensive review. *Front. Pharmacol.* **2025**, *16*, 1492517. [CrossRef]
290. Infante, R.; Infante, M.; Pastore, D.; Pacifici, F.; Chiereghin, F.; Malatesta, G.; Donadel, G.; Tesauro, M.; Della-Morte, D. An Appraisal of the Oleocanthal-Rich Extra Virgin Olive Oil (EVOO) and Its Potential Anticancer and Neuroprotective Properties. *Int. J. Mol. Sci.* **2023**, *24*, 17323. [CrossRef]
291. Chou, L.M.; Lin, C.I.; Chen, Y.H.; Liao, H.; Lin, S.H. A diet containing grape powder ameliorates the cognitive decline in aged rats with a long-term high-fructose-high-fat dietary pattern. *J. Nutr. Biochem.* **2016**, *34*, 52–60. [CrossRef] [PubMed]
292. Jaberi, K.R.; Alamdari-palangi, V.; Savardashtaki, A.; Vatankhah, P.; Jamialahmadi, T.; Tajbakhsh, A.; Sahebkar, A. Modulatory Effects of Phytochemicals on Gut–Brain Axis: Therapeutic Implication. *Curr. Dev. Nutr.* **2024**, *8*, 103785. [CrossRef] [PubMed]
293. Sánchez-Villegas, A.; Galbete, C.; Martinez-González, M.A.; Martinez, J.A.; Razquin, C.; Salas-Salvadó, J.; Estruch, R.; Buil-Cosiales, P.; Martí, A. The effect of the Mediterranean diet on plasma brain-derived neurotrophic factor (BDNF) levels: The PREDIMED-NAVARRA randomized trial. *Nutr. Neurosci.* **2011**, *14*, 195–201. [CrossRef] [PubMed]
294. Bańkowski, S.; Wójcik, Z.B.; Grabara, M.; Ozner, D.; Pałka, T.; Stanek, A.; Sadowska-Krępa, E. Does curcumin supplementation affect inflammation, blood count and serum brain-derived neurotropic factor concentration in amateur long-distance runners? *PLoS ONE* **2025**, *20*, e0317446. [CrossRef]
295. Huhn, S.; Beyer, F.; Zhang, R.; Lampe, L.; Grothe, J.; Kratzsch, J.; Willenberg, A.; Breitfeld, J.; Kovacs, P.; Stumvoll, M.; et al. Effects of resveratrol on memory performance, hippocampus connectivity and microstructure in older adults—A randomized controlled trial. *Neuroimage* **2018**, *174*, 177–190. [CrossRef]
296. O'neill Rothenberg, D.; Zhang, L. Mechanisms underlying the anti-depressive effects of regular tea consumption. *Nutrients* **2019**, *11*, 1361. [CrossRef]
297. García-Cordero, J.; Pino, A.; Cuevas, C.; Puertas-Martín, V.; San Román, R.; de Pascual-Teresa, S. Neurocognitive effects of cocoa and red-berries consumption in healthy adults. *Nutrients* **2022**, *14*, 1. [CrossRef]
298. Cimini, A.; Gentile, R.; D'Angelo, B.; Benedetti, E.; Cristiano, L.; Avantaggiati, M.L.; Giordano, A.; Ferri, C.; Desideri, G. Cocoa powder triggers neuroprotective and preventive effects in a human Alzheimer's disease model by modulating BDNF signaling pathway. *J. Cell. Biochem.* **2013**, *114*, 2209–2220. [CrossRef]
299. Volkow, N.D.; Michaelides, M.; Baler, R. The neuroscience of drug reward and addiction. *Physiol. Rev.* **2019**, *99*, 2115–2140. [CrossRef]
300. Volkow, N.D.; Morales, M. The Brain on Drugs: From Reward to Addiction. *Cell* **2015**, *162*, 712–725. [CrossRef]
301. Kauer, J.A.; Malenka, R.C. Synaptic plasticity and addiction. *Nat. Rev. Neurosci.* **2007**, *8*, 844–858. [CrossRef] [PubMed]
302. Ceci, F.M.; Ferraguti, G.; Petrella, C.; Greco, A.; Ralli, M.; Iannitelli, A.; Carito, V.; Tirassa, P.; Chaldakov, G.N.; Messina, M.P.; et al. Nerve Growth Factor in Alcohol Use Disorders. *Curr. Neuropharmacol.* **2020**, *19*, 45–60. [CrossRef] [PubMed]
303. Angelucci, F.; Ricci, V.; Pomponi, M.; Conte, G.; Mathé, A.A.; Attilio Tonali, P.; Bria, P. Chronic heroin and cocaine abuse is associated with decreased serum concentrations of the nerve growth factor and brain-derived neurotrophic factor. *J. Psychopharmacol.* **2007**, *21*, 820–825. [CrossRef] [PubMed]
304. Inal-Emiroglu, F.N.; Karabay, N.; Resmi, H.; Guleryuz, H.; Baykara, B.; Alsen, S.; Senturk-Pilan, B.; Akay, A.; Kose, S. Correlations between amygdala volumes and serum levels of BDNF and NGF as a neurobiological markerin adolescents with bipolar disorder. *J. Affect. Disord.* **2015**, *182*, 50–56A. [CrossRef]
305. Tseilikman, V.E.; Shatilov, V.A.; Zhukov, M.S.; Buksha, I.A.; Epitashvily, A.E.; Lipatov, I.A.; Aristov, M.R.; Koshelev, A.G.; Karpenko, M.N.; Traktirov, D.S.; et al. Limited Cheese Intake Paradigm Replaces Patterns of Behavioral Disorders in Experimental PTSD: Focus on Resveratrol Supplementation. *Int. J. Mol. Sci.* **2023**, *24*, 14343. [CrossRef]
306. Gu, Z.; Chu, L.; Han, Y. Therapeutic effect of resveratrol on mice with depression. *Exp. Ther. Med.* **2019**, *17*, 3061–3064. [CrossRef]
307. Chakraborty, A.K.; Tiwari, P.; Khobragade, D.S.; Kadiri, S.K.; Sheikh, I.A.; Thakur, J. The Neuroprotective Action of Resveratrol Against Cognitive Impairments Induced by Lorazepam in Male Rats. *Curr. Drug Saf.* **2024**, *20*, 341–348. [CrossRef]
308. Li, Y.; Yu, L.; Zhao, L.; Zeng, F.; Liu, Q.S. Resveratrol modulates cocaine-induced inhibitory synaptic plasticity in VTA dopamine neurons by inhibiting phosphodiesterases (PDEs). *Sci. Rep.* **2017**, *7*, 15657. [CrossRef]

309. Shuto, T.; Kuroiwa, M.; Koga, Y.; Kawahara, Y.; Sotogaku, N.; Toyomasu, K.; Nishi, A. Acute effects of resveratrol to enhance cocaine-induced dopamine neurotransmission in the striatum. *Neurosci. Lett.* **2013**, *542*, 107–112. [CrossRef]
310. Nguyen, H.D. Resveratrol, Endocrine Disrupting Chemicals, Neurodegenerative Diseases and Depression: Genes, Transcription Factors, microRNAs, and Sponges Involved. *Neurochem. Res.* **2023**, *48*, 604–624. [CrossRef]
311. Petrella, C.; Carito, V.; Carere, C.; Ferraguti, G.; Ciafrè, S.; Natella, F.; Bello, C.; Greco, A.; Ralli, M.; Mancinelli, R.; et al. Oxidative stress inhibition by resveratrol in alcohol-dependent mice. *Nutrition* **2020**, *79–80*, 110783. [CrossRef] [PubMed]
312. Petrella, C.; Di Certo, M.G.; Gabanella, F.; Barbato, C.; Ceci, F.M.; Greco, A.; Ralli, M.; Polimeni, A.; Angeloni, A.; Severini1, C.; et al. Mediterranean Diet, Brain and Muscle: Olive Polyphenols and Resveratrol Protection in Neurodegenerative and Neuromuscular Disorders. *Curr. Med. Chem.* **2021**, *28*, 7595–7613. [CrossRef] [PubMed]
313. Wu, Y.-M.; Lin, X.; Su, Y.-J.; Xue, D.; Zhang, C. Effects of curcumin on liver injury induced by chronic alcohol addiction. *Zhongguo Ying Yong Sheng Li Xue Za Zhi* **2022**, *38*, 782–786. [CrossRef] [PubMed]
314. Soltaninejad, M.; Amleshi, R.S.; Shabani, M.; Ilaghi, M. Unraveling the protective effects of curcumin against drugs of abuse. *Heliyon* **2024**, *10*, e30468. [CrossRef]
315. Bandyopadhyaya, G.; Sinha, S.; Chattopadhyay, B.D.; Chakraborty, A. Protective role of curcumin against nicotine-induced genotoxicity on rat liver under restricted dietary protein. *Eur. J. Pharmacol.* **2008**, *588*, 151–157. [CrossRef]
316. Poulose, S.M.; Miller, M.G.; Scott, T.; Shukitt-Hale, B. Nutritional factors affecting adult neurogenesis and cognitive function. *Adv. Nutr.* **2017**, *8*, 804–811. [CrossRef]
317. Kulkarni, S.K.; Bhutani, M.K.; Bishnoi, M. Antidepressant activity of curcumin: Involvement of serotonin and dopamine system. *Psychopharmacology* **2008**, *201*, 435–442. [CrossRef]
318. Chang, X.R.; Wang, L.; Li, J.; Wu, D.S. Analysis of anti-depressant potential of curcumin against depression induced male albino wistar rats. *Brain Res.* **2016**, *1642*, 219–225. [CrossRef]
319. Arora, V.; Kuhad, A.; Tiwari, V.; Chopra, K. Curcumin ameliorates reserpine-induced pain-depression dyad: Behavioural, biochemical, neurochemical and molecular evidences. *Psychoneuroendocrinology* **2011**, *36*, 1570–1581. [CrossRef]
320. Rahmadi, M.; Nurhan, A.D.; Rahmawati, R.I.A.; Damayanti, T.F.; Purwanto, D.A.; Khotib, J. Epigallocatechin Gallate Ameliorates Nicotine Withdrawal Conditions-Induced Somatic and Affective Behavior Changes in Mice and Its Molecular Mechanism. *Behav. Neurol.* **2023**, *2023*, 5581893. [CrossRef]
321. Lardner, A.L. Neurobiological effects of the green tea constituent theanine and its potential role in the treatment of psychiatric and neurodegenerative disorders. *Nutr. Neurosci.* **2014**, *17*, 145–155. [CrossRef] [PubMed]
322. Sangiovanni, E.; Brivio, P.; Dell'Agli, M.; Calabrese, F. Botanicals as Modulators of Neuroplasticity: Focus on BDNF. *Neural Plast.* **2017**, *2017*, 5965371. [CrossRef] [PubMed]
323. Meeusen, R. Exercise, nutrition and the brain. *Sport. Med.* **2014**, *44*, S47–S56. [CrossRef] [PubMed]
324. Si, Z.; Wang, X.; Yu, Z.; Ruan, Y.; Qian, L.; Lin, S.; Gong, X.; Li, L.; Huang, J.; Liu, Y. EGCG attenuates METH self-administration and reinstatement of METH seeking in mice. *Addict. Biol.* **2023**, *28*, e13307. [CrossRef]
325. Vieiros, M.; Almeida-Toledano, L.; Serra-Delgado, M.; Navarro-Tapia, E.; Ramos-Triguero, A.; Muñoz-Lozano, C.; Martínez, L.; Marchei, E.; Gómez-Roig, M.D.; Algar, Ó.G.; et al. Effects of maternal drinking patterns and epigallocatechin-3-gallate treatment on behavioural and molecular outcomes in a mouse model of fetal alcohol spectrum disorders. *Biomed. Pharmacother.* **2025**, *187*, 118138. [CrossRef]
326. Wang, Y.; Wu, S.; Li, Q.; Lang, W.; Li, W.; Jiang, X.; Wan, Z.; Chen, J.; Wang, H. Epigallocatechin-3-gallate: A phytochemical as a promising drug candidate for the treatment of Parkinson's disease. *Front. Pharmacol.* **2022**, *13*, 977521. [CrossRef]
327. Kostrzewa, R.M.; Segura-Aguilar, J. Novel mechanisms and approaches in the study of neurodegeneration and neuroprotection. A review. *Neurotox. Res.* **2003**, *5*, 375–383. [CrossRef]
328. Lerner, T.N.; Holloway, A.L.; Seiler, J.L. Dopamine, Updated: Reward Prediction Error and Beyond. *Curr. Opin. Neurobiol.* **2021**, *67*, 123–130. [CrossRef]
329. Schultz, W. Predictive reward signal of dopamine neurons. *J. Neurophysiol.* **1998**, *80*, 1–27. [CrossRef]
330. Petrella, C.; Ferraguti, G.; Tarani, L.; Chaldakov, G.N.; Ceccanti, M.; Greco, A.; Ralli, M.; Fiore, M. Olive Polyphenols and Chronic Alcohol Protection. In *Olives and Olive Oil in Health and Disease Prevention*, 2nd ed.; Preedy, V.R., Ross Watson, R., Eds.; Elsevier: Amsterdam, The Netherlands, 2021; Chapter 39, pp. 471–478.
331. Nani, A.; Murtaza, B.; Khan, A.S.; Khan, N.A.; Hichami, A. Antioxidant and anti-inflammatory potential of polyphenols contained in Mediterranean diet in obesity: Molecular mechanisms. *Molecules* **2021**, *26*, 985. [CrossRef]
332. Robles-Almazan, M.; Pulido-Moran, M.; Moreno-Fernandez, J.; Ramirez-Tortosa, C.; Rodriguez-Garcia, C.; Quiles, J.L.; Ramirez-Tortosa, M. Hydroxytyrosol: Bioavailability, toxicity, and clinical applications. *Food Res. Int.* **2018**, *105*, 654–667. [CrossRef] [PubMed]
333. Carito, V.; Venditti, A.; Bianco, A.; Ceccanti, M.; Serrilli, A.M.; Chaldakov, G.; Tarani, L.; De Nicolò, S.; Fiore, M. Effects of olive leaf polyphenols on male mouse brain NGF, BDNF and their receptors TrkA, TrkB and p75. *Nat. Prod. Res.* **2014**, *28*, 1970–1984. [CrossRef] [PubMed]

334. Carito, V.; Ceccanti, M.; Cestari, V.; Natella, F.; Bello, C.; Coccurello, R.; Mancinelli, R.; Fiore, M. Olive polyphenol effects in a mouse model of chronic ethanol addiction. *Nutrition* **2017**, *33*, 65–69. [CrossRef] [PubMed]
335. Pasban-Aliabadi, H.; Esmaeili-Mahani, S.; Sheibani, V.; Abbasnejad, M.; Mehdizadeh, A.; Yaghoobi, M.M. Inhibition of 6-hydroxydopamine-induced PC12 cell apoptosis by olive (*Olea europaea* L.) leaf extract is performed by its main component oleuropein. *Rejuvenation Res.* **2013**, *16*, 134–142. [CrossRef]
336. Achour, I.; Arel-Dubeau, A.M.; Renaud, J.; Legrand, M.; Attard, E.; Germain, M.; Martinoli, M.G. Oleuropein prevents neuronal death, mitigates mitochondrial superoxide production and modulates autophagy in a dopaminergic cellular model. *Int. J. Mol. Sci.* **2016**, *17*, 1293. [CrossRef]
337. Badr, A.M.; Attia, H.A.; Al-Rasheed, N. Oleuropein Reverses Repeated Corticosterone-Induced Depressive-Like Behavior in mice: Evidence of Modulating Effect on Biogenic Amines. *Sci. Rep.* **2020**, *10*, 3336. [CrossRef]
338. Marcelino, G.; Hiane, P.A.; Freitas, K.D.C.; Santana, L.F.; Pott, A.; Donadon, J.R.; Guimarães, R.D.C.A. Effects of olive oil and its minor components on cardiovascular diseases, inflammation, and gut microbiota. *Nutrients* **2019**, *11*, 1826. [CrossRef]
339. Pojero, F.; Aiello, A.; Gervasi, F.; Caruso, C.; Ligotti, M.E.; Calabrò, A.; Procopio, A.; Candore, G.; Accardi, G.; Allegra, M. Effects of Oleuropein and Hydroxytyrosol on Inflammatory Mediators: Consequences on Inflammaging. *Int. J. Mol. Sci.* **2023**, *24*, 380. [CrossRef]
340. Pérez-Mañá, C.; Farré, M.; Pujadas, M.; Mustata, C.; Menoyo, E.; Pastor, A.; Langohr, K.; De La Torre, R. Ethanol induces hydroxytyrosol formation in humans. *Pharmacol. Res.* **2015**, *95–96*, 27–33. [CrossRef]
341. De La Torre, R. Bioavailability of olive oil phenolic compounds in humans. *Inflammopharmacology* **2008**, *16*, 245–247. [CrossRef]
342. Hersant, H.; He, S.; Maliha, P.; Grossberg, G. Over the Counter Supplements for Memory: A Review of Available Evidence. *CNS Drugs* **2023**, *37*, 797–817. [CrossRef] [PubMed]
343. Thirumdas, R.; Kothakota, A.; Pandiselvam, R.; Bahrami, A.; Barba, F.J. Role of food nutrients and supplementation in fighting against viral infections and boosting immunity: A review. *Trends Food Sci. Technol.* **2021**, *110*, 66–77. [CrossRef] [PubMed]
344. Solfrizzi, V.; Agosti, P.; Lozupone, M.; Custodero, C.; Schilardi, A.; Valiani, V.; Sardone, R.; Dibello, V.; Di Lena, L.; Lamanna, A.; et al. Nutritional Intervention as a Preventive Approach for Cognitive-Related Outcomes in Cognitively Healthy Older Adults: A Systematic Review. *J. Alzheimer's Dis.* **2018**, *64*, S229–S254. [CrossRef] [PubMed]
345. Neshatdoust, S.; Saunders, C.; Castle, S.M.; Vauzour, D.; Williams, C.; Butler, L.; Lovegrove, J.A.; Spencer, J.P.E. High-flavonoid intake induces cognitive improvements linked to changes in serum brain-derived neurotrophic factor: Two randomised, controlled trials. *Nutr. Heal. Aging* **2016**, *4*, 81–93. [CrossRef]
346. Nehlig, A. The neuroprotective effects of cocoa flavanol and its influence on cognitive performance. *Br. J. Clin. Pharmacol.* **2013**, *75*, 716–727. [CrossRef]
347. Abdelmeguid, N.E.; Hammad, T.M.; Abdel-Moneim, A.M.; Salam, S.A. Effect of Epigallocatechin-3-gallate on Stress-Induced Depression in a Mouse Model: Role of Interleukin-1β and Brain-Derived Neurotrophic Factor. *Neurochem. Res.* **2022**, *47*, 3464–3475. [CrossRef]
348. Sloan, R.P.; Wall, M.; Yeung, L.K.; Feng, T.; Feng, X.; Provenzano, F.; Schroeter, H.; Lauriola, V.; Brickman, A.M.; Small, S.A. Insights into the role of diet and dietary flavanols in cognitive aging: Results of a randomized controlled trial. *Sci. Rep.* **2021**, *11*, 3837. [CrossRef]
349. Moriya, J.; Chen, R.; Yamakawa, J.; Sasaki, K.; Ishigaki, Y.; Takahashi, T. Resveratrol improves hippocampal atrophy in chronic fatigue mice by enhancing neurogenesis and inhibiting apoptosis of granular cells. *Biol. Pharm. Bull.* **2011**, *34*, 354–359. [CrossRef]
350. Chen, J.J.; Shen, J.X.; Yu, Z.H.; Pan, C.; Han, F.; Zhu, X.L.; Xu, H.; Xu, R.T.; Wei, T.Y.; Lu, Y.P. The Antidepressant Effects of Resveratrol are Accompanied by the Attenuation of Dendrite/Dendritic Spine Loss and the Upregulation of BDNF/p-cofilin1 Levels in Chronic Restraint Mice. *Neurochem. Res.* **2021**, *46*, 660–674. [CrossRef]
351. García-Aguilar, A.; Palomino, O.; Benito, M.; Guillén, C. Dietary polyphenols in metabolic and neurodegenerative diseases: Molecular targets in autophagy and biological effects. *Antioxidants* **2021**, *10*, 142. [CrossRef]
352. Farhan, M.; Rizvi, A. Understanding the Prooxidant Action of Plant Polyphenols in the Cellular Microenvironment of Malignant Cells: Role of Copper and Therapeutic Implications. *Front. Pharmacol.* **2022**, *13*, 929853. [CrossRef] [PubMed]
353. Rahim, R.A.; Jayusman, P.A.; Muhammad, N.; Ahmad, F.; Mokhtar, N.; Mohamed, I.N.; Mohamed, N.; Shuid, A.N. Recent advances in nanoencapsulation systems using plga of bioactive phenolics for protection against chronic diseases. *Int. J. Environ. Res. Public. Health* **2019**, *16*, 4962. [CrossRef]
354. Khatoon, S.; Kalam, N.; Shaikh, M.F.; Hasnain, M.S.; Hafiz, A.K.; Ansari, M.T. Nanoencapsulation of Polyphenols as Drugs and Supplements for Enhancing Therapeutic Profile—A Review. *Curr. Mol. Pharmacol.* **2021**, *15*, 77–107. [CrossRef]
355. Trindade, L.R.; da Silva, D.V.T.; Baião, D.D.S.; Paschoalin, V.M.F. Increasing the power of polyphenols through nanoencapsulation for adjuvant therapy against cardiovascular diseases. *Molecules* **2021**, *26*, 4621. [CrossRef]
356. Noor, N.; Gani, A.; Gani, A.; Shah, A.; Ashraf, Z. Exploitation of polyphenols and proteins using nanoencapsulation for anti-viral and brain boosting properties—Evoking a synergistic strategy to combat COVID-19 pandemic. *Int. J. Biol. Macromol.* **2021**, *180*, 375–384. [CrossRef]

357. Jayusman, P.A.; Nasruddin, N.S.; Mahamad Apandi, N.I.; Ibrahim, N.; Budin, S.B. Therapeutic Potential of Polyphenol and Nanoparticles Mediated Delivery in Periodontal Inflammation: A Review of Current Trends and Future Perspectives. *Front. Pharmacol.* **2022**, *13*, 847702. [CrossRef]
358. El-Saadony, M.T.; Yang, T.; Korma, S.A.; Sitohy, M.; Abd El-Mageed, T.A.; Selim, S.; Al Jaouni, S.K.; Salem, H.M.; Mahmmod, Y.; Soliman, S.M.; et al. Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. *Front. Nutr.* **2023**, *9*, 1040259. [CrossRef]
359. Elanthendral, G.; Shobana, N.; Meena, R.; Samrot, A.V. Utilizing pharmacological properties of polyphenolic curcumin in nanotechnology. *Biocatal. Agric. Biotechnol.* **2021**, *38*, 102212. [CrossRef]
360. Cas, M.D.; Ghidoni, R. Dietary curcumin: Correlation between bioavailability and health potential. *Nutrients* **2019**, *11*, 2147. [CrossRef]
361. Górnicka, J.; Mika, M.; Wróblewska, O.; Siudem, P.; Paradowska, K. Methods to Improve the Solubility of Curcumin from Turmeric. *Life* **2023**, *13*, 207. [CrossRef]
362. Hegde, M.; Girisa, S.; BharathwajChetty, B.; Vishwa, R.; Kunnumakkara, A.B. Curcumin Formulations for Better Bioavailability: What We Learned from Clinical Trials Thus Far? *ACS Omega* **2023**, *8*, 10713–10746. [CrossRef] [PubMed]
363. Bansal, S.S.; Goel, M.; Aqil, F.; Vadhanam, M.V.; Gupta, R.C. Advanced drug delivery systems of curcumin for cancer chemoprevention. *Cancer Prev. Res.* **2011**, *4*, 1158–1171. [CrossRef] [PubMed]
364. Wang, S.; Wang, J.; Chen, Z.; Luo, J.; Guo, W.; Sun, L.; Lin, L. Targeting M2-like tumor-associated macrophages is a potential therapeutic approach to overcome antitumor drug resistance. *npj Precis. Oncol.* **2024**, *8*, 31. [CrossRef] [PubMed]
365. Muzio, L.; Viotti, A.; Martino, G. Microglia in Neuroinflammation and Neurodegeneration: From Understanding to Therapy. *Front. Neurosci.* **2021**, *15*, 742065. [CrossRef]
366. Abe, N.; Nishihara, T.; Yorozuya, T.; Tanaka, J. Microglia and Macrophages in the Pathological Central and Peripheral Nervous Systems. *Cells* **2020**, *9*, 2132. [CrossRef]
367. Miyamoto, Y.; Kubota, K.; Asawa, Y.; Hoshi, K.; Hikita, A. M1-like macrophage contributes to chondrogenesis in vitro. *Sci. Rep.* **2021**, *11*, 21307. [CrossRef]
368. Yamasaki, R. Elucidation of the role of microglia-macrophage-based neuroinflammation in neurological diseases. *Neurol. Clin. Neurosci.* **2024**, *12*, 329–339. [CrossRef]
369. Wes, P.D.; Holtman, I.R.; Boddeke, E.W.G.M.; Möller, T.; Eggen, B.J.L. Next generation transcriptomics and genomics elucidate biological complexity of microglia in health and disease. *Glia* **2016**, *64*, 197–213. [CrossRef]
370. Nakaso, K. Roles of Microglia in Neurodegenerative Diseases. *Yonago Acta Med.* **2024**, *67*, 1–8. [CrossRef]
371. Jie, S.; Fu, A.; Wang, C.; Rajabi, S. A comprehensive review on the impact of polyphenol supplementation and exercise on depression and brain function parameters. *Behav. Brain Funct.* **2025**, *21*, 10. [CrossRef]