

Nutritional and Dietary Considerations for Basal Ganglia Disorders

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Abstract

Various flavonoids, botanicals, nutrients, amino acids, sulfur compounds, pro-glutathione compounds have been shown to dampen the oxidative stress mechanisms of basal ganglia disorders in addition to various models of basal ganglia neurodegenerative mechanisms. Dietary associations with gluten sensitivity, celiac disease, caloric restriction, and intermittent fasting have also been evaluated in the dietary model of basal ganglia neurodegeneration. This article will review these nutritional and dietary interventions with basal ganglia disease.

Keywords: Basal Ganglia, Flavonoids, Botanicals, Nutrients, Amino Acids, Glutathione, Gluten Sensitivity, Caloric Restriction

Introduction

Disorders of the basal ganglia such as Parkinson's, dystonia, tics, restless leg syndrome, obsessive compulsive disorders, and numerous movement and cognitive disorders are common conditions in the current population however the use of dietary and nutritional supplementation has not been routinely implemented in the management of these conditions in the current healthcare model.

The use of antioxidants either with dietary restrictions or nutrient supplementation has demonstrated potential

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Flavonoids with Basal Ganglia Protective Properties

Flavonoids are a family of antioxidants found in fruits, vegetables, spices, and teas. The physiological benefits of flavonoids have been largely attributed to their antioxidant properties in quenching the energy-linked excitotoxic model of neurodegeneration. Nerve cell death from oxidative stress has been implicated in basal ganglia diseases. In addition to antioxidant properties, flavonoids have demonstrated three separate mechanisms of protection. These include increasing intracellular glutathione, directly lowering levels of reactive oxygen species, and preventing the influx of Ca²⁺ despite high levels of reactive oxygen species [3].

The following list of flavonoids have all demonstrated basal ganglia protective properties and are found in foods, spices, teas and are isolated as nutritional supplements. The flavonoids include lycopene [4], quercetin [5-7], biacalein [8-11], curcumin [12-14], resveratrol [15-23], apigenin [24], spirulina [25], luteolin [26], and grape seed extract [27].

Botanicals with Basal Ganglia Protective Properties

Botanicals are any plants "with leaves, seeds, or flowers used for flavoring, food, medicine, or perfume" or parts of "such a plant as used in cooking." Botanicals have been used in almost all ancient cultures for medicinal purposes. Over the years the scientific community has evaluated the effects and physiological mechanisms of medicinal compounds that have led to better understanding of mechanisms of action, dosage, and clinical use. Numerous botanical compounds have been studied and

validated as effective treatment modalities in basal ganglia disease. The mechanism of action involves their ability to raise antioxidants, improve blood flow, dampen microglia neuroinflammation, protect the mitochondria, modulate nitric oxide isomer expression, and reduce oxidative stress by various known and unknown mechanisms. The botanicals that have demonstrated specific protection for the basal ganglia include, green tea polyphenols [28-38], hibiscus asper leaves [39], hyoscyamus niger seeds [40], rosmarinic acid [41], silymarin [42,43], mulberry fruit extract [44], centella asiatica [45], grape seed extract [46], withania somnifera [47], ashwaganda [48], and ginseng [49,50].

Nutrients with Basal Ganglia Protective Properties

Several nutrients possess antioxidant properties and act as cofactors for mitochondrial energy function have shown protective properties specifically for basal ganglia neurodegeneration. These nutrients include CoQ10 [51-56], tocopherols [57-59], folate [60], and zinc [61].

Iron Deficiency and Basal Ganglia Disorders

Iron is an essential mineral necessary for many physiological processes and is also one of the most common nutritional deficiencies worldwide. Iron deficiency and anemia have been associated with various mechanisms of basal ganglia degenerative disease. Iron deficiency has been associated with manganese accumulation in the basal ganglia leading to neurotoxicity. Particularly, iron-deficiency seems to be frequent among patients showing brain MRI

abnormalities compatible with manganese deposits in basal ganglia. This observation suggests that iron-deficiency could be an important risk factor for manganese-induced neurotoxicity and should, therefore, be accurately considered and treated [62].

Iron deficiency has also been associated with formation of blood clots in the cerebral veins leading to small vascular lesions in the basal ganglia. Additionally impaired absorption of iron by the neuromelanin cells in the basal ganglia may be associated with restless leg syndrome [63,64].

Iron deficiency has also been associated with dopamine system functioning. Children and young adults who had iron deficiency anemia in infancy show poorer inhibitory control and executive functioning as assessed by neurocognitive tasks where pharmacologic and neuroimaging studies implicate frontal-striatal circuits and the mesocortical dopamine pathway [65].

Research conducted using tissue autopsy of the substantia nigra and putamen from individuals with primary restless leg syndrome and neurologically normal control groups concluded that primary iron insufficiency has been shown to produce a dopaminergic abnormality characterized as an overly activated dopaminergic system as part of restless leg syndrome pathology [66].

Amino Acids and Sulfur Compounds with Basal Ganglia Protective Properties

Amino acids are molecules containing an amine group, a carboxylic group, and a side chain that is specific to the amino acid. Sulfur based amino acids such as N-acetylcysteine and sulfur compounds such as alpha lipoic acid have been shown to be protective for basal ganglia degenerative disease. Additionally, the amino acid L-

carnitine used for mitochondrial energy production has demonstrated basal ganglia protective properties as have N-acetylcysteine [67-71], alpha lipoic acid [72,73], L-carnitine [74].

Dietary Gluten and Celiac Disease Associations with Basal Ganglia Disease

Several disease have linked various basal ganglia disorders with dietary gluten and celiac disease such as paroxysmal nonkinesigenic dyskinesias, multiple systems atrophy, vascular dystonia, and Parkinson's disease [75-78]. Gluten sensitivity is a systemic autoimmune disease that occurs in genetically susceptible individuals on ingesting gluten. Although it was initially associated with disease and destruction of the intestinal mucosa recent research has shown that gluten sensitivity can be exclusively a neurological disease [79]. Neurological manifestations of gluten sensitivity, with or without enteropathy, are also frequent, their pathogenesis including an immunological attack on the central and peripheral nervous tissue accompanied by neurodegenerative changes.

The early detection of cases of gluten sensitivity with neurological manifestations and subsequent treatment with the gluten-free diet has shown to provide remarkable benefits to the patients with gluten sensitivity [80].

Glutathione and Basal Ganglia Disorders

Glutathione is an important intercellular antioxidant and has shown an intimate relationship with mitochondrial dysfunction and reactive oxygen species reactions found

in neurodegenerative disorders such as basal ganglia degenerative diseases [81-83]. Alterations in glutathione metabolism have been shown to lead to alterations in mitochondrial function and the production of reactive oxygen species. These changes cause alterations in the mitochondrial transmembrane potential which is the initiating step in the neuroexcitotoxic mode [84-85]. Cell culture studies using immature cortical neurons demonstrated depletion of glutathione triggers the activation of neuronal 12-lipoxygenase, which leads to the production of peroxides, the influx of calcium, and ultimately to cell death [86].

Glutathione is found in a variety of foods that include fruits, vegetables, and meats. There are numerous antioxidants, foods, flavonoids and botanicals associated with basal ganglia neurodegeneration protection appear to impact increased production of glutathione levels.

There are many natural compounds that have been shown to increase glutathione levels and may have potential to quench the oxidative stress associated with basal ganglia degenerative disease.

N-Acetyl Cysteine (NAC) is a metabolite of the sulfur-containing amino acid, Cysteine. It plays a role in the sulfation cycle, acting as a sulfur donor in phase II detoxification and as a methyl donor in the conversion of homocysteine to methionine. N-Acetyl Cysteine is rapidly metabolized to intracellular glutathione. It is used medically for acetaminophen overdose and as a nephroprotective agent for radiocontrast [87-95].

Alpha lipoic acid is an antioxidant that is made by the body and is significantly increased where it helps turn glucose into energy. It directly recycles and extends the metabolic life spans of vitamin C, glutathione, and coenzyme Q10, and it indirectly renews vitamin E [96-110].

Glutathione is a tripeptide consisting of glutamate, cysteine, and glycine. Research has demonstrated that glutamate is a conditional essential

amino acid that plays a central role in response to oxidative stress and glutathione demands [111-124].

Selenium is a trace element nutrient that serves as the essential cofactor for the enzyme glutathione peroxidase. Glutathione peroxidase is the general name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage. The biochemical function of glutathione peroxidase is to reduce lipid hydroperoxides to their non-destructive end products. Selenium-deficient humans and animals are known to be deficient in glutathione peroxidase (GSHPx) [125-130].

Cordyceps is a traditional Chinese herb that possesses anti-tumour, anti-oxidation and immune modulating properties. It has been shown to activate both glutathione peroxidase and superoxide dismutase enzymes as well as increase their amounts in the body. Cordyceps research has demonstrated it protects cells by engaging the glutathione enzyme cycle [140-143].

Centella asiatica is a common medicinal plant in ayurvedic medicine to treat various chronic diseases. In the scientific literature it is becoming researched extensively for its neuroprotective and wound healing properties. Research has clearly demonstrated that oral intake very rapidly and dramatically increases the activity and amount of glutathione peroxidase and the quantity of glutathione [144-155].

Silybum marianum has classically been used to support liver disorders. Administration of Silybum marianum has been shown to significantly increase glutathione, increase superoxide dismutase activity, and have positive influence in the ratios of reduced and oxidized glutathione [156-172].

Caloric Restriction, Neuroprotection and the Basal Ganglia

Caloric restriction and intermittent fasting have been shown to provide neuroprotective activities by reducing free radical promoted oxidative stress responses leading to mitochondrial failure and activation of the energy-linked excitotoxic model of neurodegeneration. Additionally, there are multiple interactive pathways and molecular mechanisms by which caloric restriction benefit neurons including those involving insulin-like signaling, FoxO transcription factors, sirtuins and peroxisome proliferator-activated receptors. These pathways stimulate the production of protein chaperones, neurotrophic factors and antioxidant enzymes, all of which help cells cope with stress and resist disease [173]. Animal studies have demonstrated specific basal ganglia protective responses from caloric restriction related to reduced basal ganglia iron deposition and also greater preserved dopamine neuron integrity with neurotoxin induced parkinsonism [174,175].

Discussion

The use of nutrients, amino acids, sulfur compounds, botanicals, and flavonoids demonstrated great potential as adjunctive aids in basal ganglia neuroprotection. These compounds can be found in antioxidant rich fruits, vegetables and spices. These compounds can also be taken in concentrated nutritional supplements to achieve natural medicinal impacts that may be difficult to reach with diet alone. These compounds have been used as food items in various cultures for hundreds of years and appear to be safe. There are no reported contraindications for these compounds in the

current scientific literature specific to basal ganglia disease, however potential adverse reactions with various drugs should be evaluated especially when using botanicals that have multiple and diverse chemical properties. Dietary associations with basal ganglia disease and gluten are being reported more in recent years and clinical screening for gluten sensitivity and celiac disease should be considered when developing dietary plans. Additionally, dietary caloric restriction and intermittent fasting may provide protective impacts on basal ganglia neurodegenerative disease. The combination of a diet rich in natural antioxidants, nutritional supplementation, gluten-free diet, with caloric restriction may provide important protective strategies for those suffering from basal ganglia degenerative disease.

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