The Benefits of Neuroids/Neuropeptides in Combating Cerebrovascular, Neurological and Ocular Diseases

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Abstract

Neuroids and neuropeptides (ND/NPs) are drugs with promising efficacy in cerebrovascular diseases. In this article the benefits and mechanisms of action of ND/NPs for stroke are reviewed in light of the pathogenesis of stroke. The primary mechanism is that ND/NPs help in the synthesis of acetylcholine and betaine. These, in turn, work to help in the formation of nerve cell membrane phospholipids and attenuate the production of free radicals. This is important in stroke because brain damage after stroke is associated with excess production of free radicals. Furthermore, ND/NPs may stimulate the activity of glutathione reductase and have the ability to promote learning and improve cognitive impairment. Pharmacokinetics suggests that ND/NPs are well absorbed, with a higher degree of bioavailability when administered orally. A dose of 500 mg to 2,000 mg per day in slow releasing form is an effective regimen based on clinical trials, and is safe for use in elderly population and pediatrics.

Index terms— betaine, choline, citicoline, neurological dysfunction, neuroids, neuroprptides, phosphatidylcholine.

1 Introduction

euroids and neuropeptides (ND/NPs) are brain chemicals and small proteinaceous substances with wide-ranging efficacy for cerebrovascular diseases associated with trauma, intoxication, drug interactions, and aging (1).

Biochemically, ND/NPs work together in the synthesis of cell membrane compounds (e.g., phosphatidylcholine, Betaine) that generate phospholipids (2). ND/NPs also attenuate the production of free radicals, promote learning, and improve cognitive impairment in brain atrophy (3). The purpose of this article is to present a brief review of the mechanisms and benefits of ND/NPs for neurological disease, especially in preventing brain injury after stroke. First, we present a brief pathogenesis of stroke, including information on diagnosis and treatment, to situate the following text on ND/NPs.

2 II.

3 Oxidative Stress in Stroke

Stroke is associated with oxidative stress, through an excessive generation of reactive oxygen species (O2S) by mitochondria (4). Excessive O2S generation is the main cause of oxidative stress. Enzymes such as nicotinamide adenine dinucleotide phosphate oxidase(NADPase) have recently been recognized and studied as important producers of O2S in brain tissues after stroke. NADPase causes neuronal inflammation and necrosis and plays an important role in brain injury after stroke (5). The enzyme is classically considered as a key part of the electron transport chain in the plasma membrane. In the process of oxidation, it produces O2S by reducing one electron in molecular oxygen and turning out a series of secondary products (such as ozone, singlet oxygen, hydrogen peroxide, hydroxyl radical, superoxide, and sodium hypochlorite) (5). These molecules, also known as free radicals, are the main source of oxidative stress disseminated in the cerebral tissues and vasculature. NADPase moieties are also found in the non-phagocytic cells and sustain low levels of activity even without extracellular stimulation. The enzymes persistently serve as electron donors to produce OS2 (6).

Several clinical pharmaceutical studies have established that NADPase inhibitors improve brain injury and improve neurological outcome after stroke. NADPase enzymes contribute to the progression of brain injury after ischemic stroke. NADPase plays a role in nerve growth factor (NGF) induced neuronal differentiation of PC12 cells, while O2S produced by NADPase help to regulate development of neuronal cells (7). However, excessive O2S production after stroke can lead to brain injury. Therefore, prevention of post-stroke brain injury via NADPase inhibitors or via compounds that protect against damage from O2S is important.

4 III.

5 Diagnosis of Stroke

A stroke patient may present with any of a range of symptoms, including the following:

? An abrupt onset of weakness/numbness in the face, arms, or legs, especially on one side of the body.

6 ND/NP Mechanisms of Action

For several years ND/NPs have been known for their promising action in biomedical sciences. ND/NPs include choline, ribose, pyrophosphate, cytosine, and peptides (8). These are essential intermediary ingredients in the synthesis of cell membrane phospholipids (Phospitadylcholines), a primary neurotransmitter (9). The latter are integral cell constituents and have a high yield rate, which entails a constant production of these constituents to guarantee the satisfactory function of cell membranes (10). As shown in Figure 1, ND/NPs function by generating phospholipids, including cytidine, choline, and neuropeptides. These promote synthesis and repair of nerve cell membranes, as well as removal of fatty acids and other degradation products at the site of nerve damage. The result is improved nerve function, including mood and memory improvements.

In the treatment of ischemia for prevention of brain stroke, ND/NPs delays the deposition of free fatty acids and formation of free radicals at the site of ischemia, thus preventing the start of proinflammatory cascades of episodes (11). This occurs through breakdown of cerebral phospholipids, exerting a protective effect upon the cell membrane ATPase and enzymes (succinyl dehydrogenase and citrate synthetase) drawn in brain energy metabolism.

In the brain, ND/NPs are the most varied class of signaling molecules involved in several physiological functions. As of today, over 70 associated genes have been identified (12). These are traced to decisive bioactive neuropeptides working in the nervous system. ND/NPs excite chemical signals, which in turn induce neurosecretion of peptide hormones in the endocrine system through sensitive nerve endings in the hypothalamus (13). ND/NPs are widely available as approved drugs for the treatment of neurological disorders. On administration, these drugs are hydrolyzed in the intestinal tract and in circulation, form useful neurogenic products such as cytidine, choline, and others (14).

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8 Benefits for Neurological Disease

ND/NPs have been revealed to work as a dopaminergic receptor agonist, inducing monoamines, serotonin, nor epinephrine, and glutamate/GABA at muscarinic site (16). Thereby, ND/NPs have been found to endorse learning and advance cognitive impairment in Parkinson's and Alzheimer's diseases (17). In addition, these neuroids lessen the severity of mental and motor insufficiency related to head injuries and support eye and mental health by improving phospholipid metabolism (18). ND/NPs help in the developenent of reduced axonal flow of dopamine. Owing to its ability to repair neuronal membranes and its ability to augment central nervous system dopamine levels, ND/NPs have been considered for the treatment of neuronal disrepair caused by infectious agents (19).

Neurological issues in the face and extremities are also of interest, because ND/NPs can be of benefit in myasthenia graves, ocular/extraocular paresis (meosis, proptosis), facial nerves palsy, diabetes, polyneuropathies, attention deficit/hyperactivity disorder (ADHD) and restless leg syndrome. Neurosecretion of acetylcholine by the ND/NPs causes helpful stimulation of small muscles in the eyes. Secretion of neurotransmitters in individuals treated with ND/NPs leads to variable degrees of improvement in muscle nerve function (20). With follow up, the resultant improvement in muscle contraction from ND/NPs treatment was been more encouraging than placebo (21). As such, ND/NPs may be used to increase acetylcholine levels and improve muscle contraction or movement (22). Thus, ND/NPs causes hormone increases (acetylcholine and derivatives) by acting to inhibit cholinesterase, the enzyme that destroys acetylcholine, at the nerve-muscle junctions (23).

ND/NPs have been found to have a levodopasparing effect and an ability to increase dopamine synthesis. Higher doses of ND/NPs (.5 g-1g) for 15 days have thus shown favorable effect on eye health, in particular for amblyopia and glaucoma (24). Glaucoma is considered a neurodegenerative disease, further supporting the role of ND/NPs in its treatment and prevention.

V.

9 Conclusion

ND/NPs are unique compounds possessing wide-ranging benefits in diseases associated with neurological disorders, cerebrovascular disorders, and ocular disorders (25). They uphold neural health and good cognitive function while suppressing the damaging effects of free radicals and boosting antioxidant mechanisms in the body. In addition, ND/NPs can advance anti-inflammatory activities and energize neurotransmitter related activities (26). Therefore, these compounds are of continued interest both clinically and for research. In addition to preventing brain damage after stroke, ND/NPs have promising applications for a range of neurological disorders.

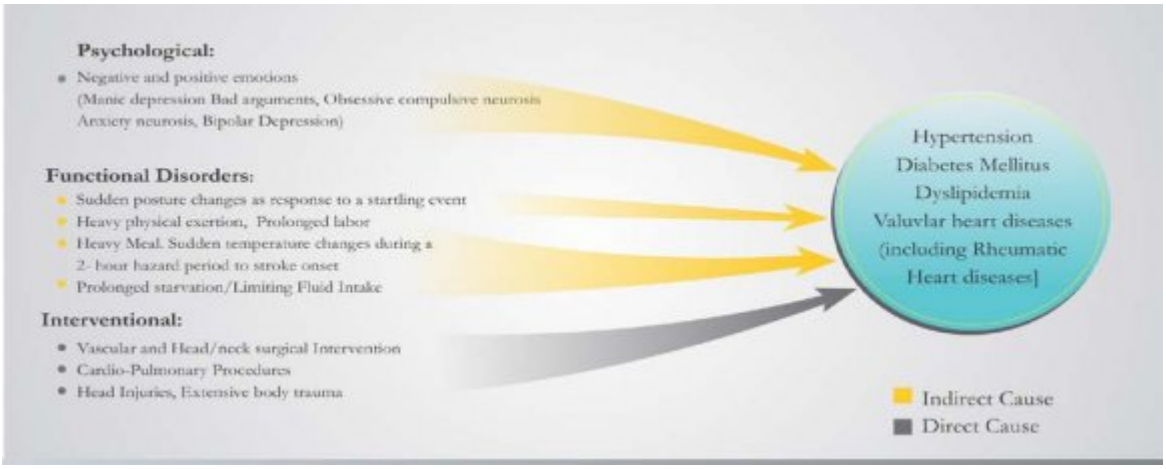

Figure 1:

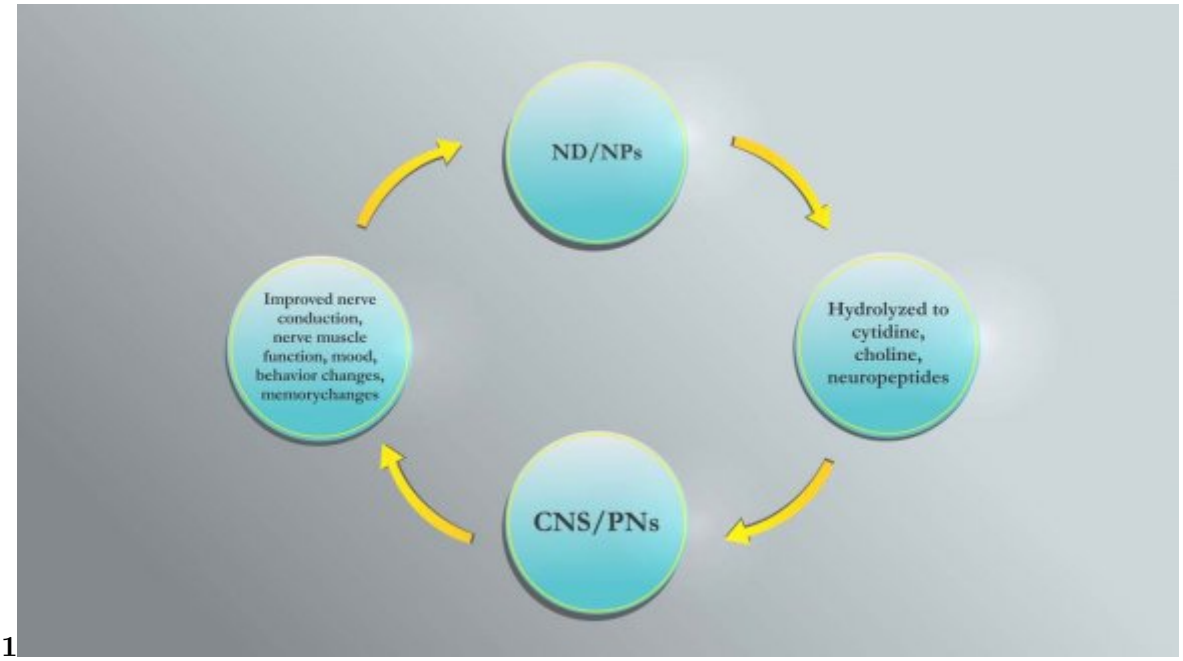

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Figure 2: Figure 1 :

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