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Editorial

Neuronal Protective Effect of Nosustrophine in Cell Culture Models

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The role of nootropic supplements is becoming increasingly relevant in today's integrated therapeutic landscape.[1] The choice of adjunctive therapy is increasingly complex because of the increasingly elaborate nature of the drugs and, consequently, the potentially resulting drug interactions. The use of a nootropic, although it has an active component, turns out to be less disruptive overall because of the fewer interactions resulting from its very nature; another aspect not to be underestimated is the general propensity of the patient to take a product to which he or she does not attribute the exact nature as the drug generally used in therapy, and this allows the clinician to be able to administer an effective add-on with good compliance on the part of the patient.[2] Among nootropic supplements, Nosustrophine has an important role. The effects of this supplement are manifold, and currently, its use is found in the treatment of Alzheimer's disease (AD). Among pharmacological interventions, the most widely used in AD are natural products (25.6%), followed by anti-amyloid beta compounds (13%), neurotransmitter enhancers (11.4%), multitarget drugs (2.5%), and antitau drugs (2.3%).[3]

Nootropic supplements are composite preparations that help to enhance multiple areas of neuronal function, such as concentration, memory, cognitive attention, and motivation while strengthening cognitive functions in patients affected by multiple neurodegenerative diseases.[4] Delving deeper into the evaluation of the neurobiological aspects of nootropics, we can highlight that fractionated catecholamines and serotonin were found in the Nosustrophine extract using ultra-high performance liquid chromatography (UHPLC) with electrochemical detection (ECD).[5]

On deep biochemical evaluation, it emerges how Nosustrophine extracts contain brain-derived neurotrophic factors and multiple neurotransmitters, particularly dopamine, norepinephrine, and serotonin. It is well known that there is a correlation between the pathogenesis and course of AD and reduced brain concentrations of dopamine, norepinephrine, and serotonin.[6] Moreover, this emphasizes AD and a wide range of pathologies affecting the neurons and the brain, including psychiatric pathologies.

Laboratory data emphasizing the effects of Nosustrophine on microglia and multiple brain formations have shown that in aged mice, Nosustrophine promotes the expression of SIRT1. Furthermore, overexpression of SIRT1 may lead to neurodegeneration, with the implication of beta-amyloid and tau pathology potentially through deacetylation of histone H3 and dysfunction at the mitochondrial level.[7]

Various natural compounds protect against neurodegeneration and contain epinutraceutical properties[8] and, starting from this, the wide range of uses that could be fulfilled in neurobiology by nootropics, particularly by Nosustrophine, becomes apparent.

Furthermore, assessing the effects on neuronal plasticity reveals how Nosustrophine is responsible for effective regulatory activity of histone deacetylases with the improvement of neuroplasticity and consequent restoration of functions, such as learning and short- and long-term memory. In patients with AD, these neuroprotective aspects imply a regulatory and limiting role of processes aimed at microstructural degeneration of the neuron and its more refined functions.[9] It seems important to emphasize the role these findings might have in preventing and treating add-ons but not limited to all those diseases with a mnesic component, either from neurodegeneration or environmental demand overload, including multiple forms of depression and psychosis.

The reviewed article presents a strength in applying Nosustrophine to novel models, such as HepG2 hepatocarcinoma and SHSY5Y neuroblastoma cells. The highlighted therapeutic properties, particularly concerning dopaminergic neural leakage, and reduction of neuroinflammation, are accompanied by considerable evidence of increased neuroprotection, giving this compound possibilities in a future perspective as a protective factor not only in AD but also in other neurodegenerative diseases, such as Parkinson disease and multiple sclerosis.

Its limitations lie in the very nature of the work. However, the study was conducted with great rigor and precision. The applicability of the cell culture model necessitates confirmation of the data and a move to the following stages of experimentation up to human subjects. The article appears novel and significant in its scope by filling in the gaps in the literature inherent in the application of Nosustrophine, which has so far focused on alternative models. At present, there are no effective therapeutics available for neurodegenerative disorders.[10] It similarly shows how various studies address the usefulness of Nosustrophine, particularly Carrera *et al*.[11] highlight its usefulness as an effective therapy using nootropic supplements against degenerative diseases, while several authors delve into deeper cellular and molecular mechanisms,

Abbreviations: AD, Alzheimer's disease; UHPLC, ultra-high performance liquid chromatography; ECD, electrochemical detection.

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reflexively highlighting its validity as exerts substantial epigenetic effects against AD-related neurodegeneration.[12,13] Particularly in their work, Carrera *et al*.[14] effectively illustrate the neuronal protective effect of Nosustrophine in cell culture models by highlighting how this is an epigenetic bioproduct derived from the brain of *Sus scrofa* domesticus using nondenaturing biotechnological processes on the progression of neurodegeneration in human neuroblastoma cell line SH-SY5Y.

The data obtained in the laboratory, and particularly *in vitro*, show that Nosustrophine contributes to the prevention of dopaminergic neuron loss in the central nervous system, with an essential role at the neurobiological level in the course of diseases such as schizophrenia and psychotic spectrum disorders. The neuroprotective activity that is exercised directly and indirectly with the support of neuroplasticity, implies application for the prevention and treatment of neuroinflammation. This highlights how Nosustrophine may be useful for the prevention of toxic neuroinduction and environmental effects in the genesis of multiple psychopathological and neurological disorders.

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Conflict of interest

Dr. Massimo Tusconi has been an editorial board member of *Journal of Exploratory Research in Pharmacology* since July 2016. The author has no other conflict of interests to declare.

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