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NEW EFFECTIVE THERAPEUTIC APPROACHES TO CONTROL NEUROINFLAMMATION IMPROVE SEVERAL NEUROPATHOLOGIES

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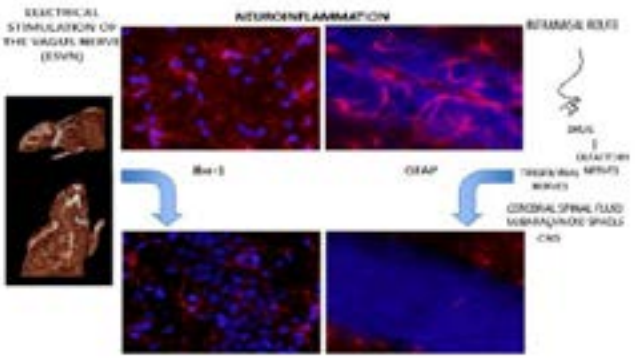
Statement of the Problem: Even though acute, transient neuroinflammation (NI) is a beneficial defensive response to harmful stimuli, sustained NI can lead to pathological conditions. NI is a common trait in many infectious and non-infectious neurological diseases and may promote their onset and progression. Its role in sepsis, Parkinson disease, stroke, and multiple sclerosis places NI as a new common therapeutic target. Controlling subacute and chronic NI may help to restore CNS physiology and homeostasis; however, NI is currently treated only during multiple sclerosis crises, being unattended in other diseases. The absence of an adequate anti-inflammatory response may explain the scarce research on this approach.

Methodology & Theoretical Orientation: The potential of electric stimulation of the vagus nerve (ESVN) and intranasal administration of glucocorticoids were studied in models of sepsis (LPS-treated mice), Parkinson disease (induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, MPTP), ischemic stroke (induced by middle cerebral artery occlusion, MCAO), and multiple sclerosis (autoimmune encephalomyelitis elicited by the myelin oligodendrocyte glycoprotein peptide 35-55).

Findings: Both ESVN and intranasal steroid administration effectively reduced central levels of TNFα, IL-1β, and IL6 (measured by ELISA) and the percentage of CD11b+/CD45 macrophages/microglial cells (measured by FACS). ESVN also reduced the expression of Iba-1 in the cortex and hippocampus. ESVN reduced astrocyte activation (GFAP) and restored the expression of tyrosine-hydroxylase (TH)-positive neurons in the substantia nigra pars compacta (SNc). Intranasal administration of dexamethasone significantly reduced mortality in the stroke model. Moreover, intranasally-treated mice exhibited lower morbidity and central inflammation, and a reduced size of the ischemic lesions. In multiple sclerosis, the intranasal route was more effective than intravenous in improving EAE-associated morbidity.

Conclusion & Significance: Our results highlight the possibility of reducing NI in several neuropathologies, restoring homeostasis more efficiently than current treatments.



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