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Chronic cuffing of cervical vagus nerve inhibits efferent fiber integrity in rat model

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Associated Data

Abstract

Objective

Numerous studies of vagal nerve stimulation (VNS) have been published showing it to be a potential treatment for chronic inflammation and other related diseases and disorders. Studies in recent years have shown that electrical stimulation of the vagal efferent fibers can artificially modulate cytokine levels and reduce systematic inflammation. Most VNS research in the treatment of inflammation have been acute studies on rodent subjects. Our study tested VNS on freely moving animals by stimulating and recording from the cervical vagus with nerve cuff electrodes over an extended period of time.

Approach

We used methods of electrical stimulation, retrograde tracing (using Fluorogold) and post necropsy histological analysis of nerve tissue, flow cytometry to measure plasma cytokine levels, and MRI scanning of gastric emptying. This novel combination of methods allowed examination of physiological aspects of VNS previously unexplored.

Main results

Through our study of 53 rat subjects, we found that chronically cuffing the left cervical vagus nerve suppressed efferent Fluorogold transport in 43 of 44 animals (36 showed complete suppression). Measured cytokine levels and gastric emptying rates concurrently showed nominal differences between chronically cuffed rats and those tested with similar acute methods. Meanwhile, results of electrophysiological and histological tests of the cuffed nerves revealed them to be otherwise healthy, consistent with previous literature.

Significance

We hypothesize that due to these unforeseen and unexplored physiological consequences of the chronically cuffed vagus nerve in a rat, that inflammatory modulation and other vagal effects by VNS may become unreliable in chronic studies. Given our findings, we submit that it would benefit the VNS community to re-examine methods used in previous literature to verify the efficacy of the rat model for chronic VNS studies.

Keywords: vagus nerve stimulation, inflammation, chronic implantation, fluorogold, flow cytometry, cuff electrode, gastric emptying