Activation of human vagus nerve afferent projections via electrical stimulation of external ear: fMRI evidence

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Introduction

The goal of the present study is to ascertain, with the use of fMRI, whether electrical stimulation of the concha, which is innervated by (the sensory) auricular branch of the vagus nerve, activates the solitary nucleus (NTS) and its projections. This would validate the use of ear stimulation as a more accessible, less invasive method of stimulating the vagus nerve. Invasive and non-invasive vagus nerve stimulation has been used against depression, epilepsy, and pain.1-11

There is anatomical evidence that a branch of the vagus nerve provides sensory innervation of the external ear. More specifically, the auricular branch of the vagus innervates the concha, which is the conical region immediately superior to the external meatus of the ear (Figure 1).

Methods

Research Participants

Seven healthy participants (5 females; 2 males; age 21-71) were recruited for the study by word of mouth. The study was approved by the Rutgers University Institutional Review Board, and the Rutgers University Brain Imaging Center (RUBiC). Participants were compensated $150.

Experimental Paradigm

Scan 1 - Control: The following fMRI data were collected in 21-min sessions: 2 min rest; 1 min basilar right-handed finger tap (10 s on/off); 7 min left auricular concha stimulation; 2 min rest; 1 min 2-cycle 2Hz stimulation; 2 min rest.

Scan 2 - Experimental: The following fMRI data were collected in 20-sec stimulation blocks: 2 min rest; 7 min concha stimulation; 1 min rest.

Before each scan, participants were fitted with Cerbomed’s NEMOS® neurostimulator device (Figure 2), a transcutaneous vagus nerve stimulator designed by Cerbomed GmbH, Erlangen, Germany. During each scan the stimulator cable was passed through a wave guide to the subject in the monitor room and the 20’ response of the hippocampus to concha stimulation was strongly confirmed by fMRI evidence that the NTS was activated by concha stimulation. This is consistent with the reported antiepileptic, antinociceptive effects of stimulation of the auricular branch of the vagus nerve12 that has been shown to provide a rational basis for the reported antiepileptic, antinociceptive effects of stimulation of the auricular branch of the vagus nerve.

Results

As summarized in the brain images:

Electrical stimulation of the concha produced activation of the following regions (based on analysis of concha stimulation minus earlobe [sham] stimulation): solitary nucleus (NTS) and its following projections: parabrachial nucleus, nucleus accumbens, hypothalamus, thalamus, amygdala. In addition, parabrachial lobule, and insula were activated.

Deactivation, based on analysis of concha against baseline, was observed in hippocampus.

Electrical stimulation of the earlobe produced activation of the following regions (based on analysis of earlobe stimulation minus concha stimulation): hippocampus, parietal, thalamus, small (non-genital) region of the paracentral lobule.

Deactivation, based on analysis of shaming against baseline, was seen in nucleus accumbens, paracentral lobule, and thalamus.

Discussion

Electrical stimulation of the concha activates the NTS and its known projections.1-11 Specifically: parabrachial nucleus, nucleus accumbens, hypothalamus, and amygdala. Additional activations were seen in the insula and paracentral lobule (genital areas of the sensory cortex).

Electrical stimulation of the external ear exerts physiological effects comparable to those elicited by invasive stimulation of the main vagus trunk in the neck, specifically against epilepsy, pain and depression.1-11,14,20,21 This and other evidence is extremely consistent with the anatomical and physiological data which show that electrical stimulation of the vagus nerve projects to the spinal trigeminal nucleus, not to NTS.5,6 (Figure 4a). However, the functional activation of the NTS may not be limited to the classical trigeminal projections; for the 2 nuclei are adjacent and, therefore, it is possible that activity that is relayed to spinal trigeminal nucleus could spread to the NTS. The right and left relayed activity in the brain stem could account for the non-physiological nature of the electrical stimulation.

A striking finding was the diametrically opposite response of the hippocampus to concha stimulation versus earlobe stimulation. This is consistent with the reported antiepileptic, antinociceptive effects of stimulation of the auricular branch of the vagus nerve that has been shown to provide a rational basis for the reported antiepileptic, antinociceptive effects of stimulation of the auricular branch of the vagus nerve.

The present finding that the septum is activated by concha stimulation suggests that this is an access route from NTS to hippocampus. Previous research provided evidence that the vagus nerve conveys vagal and cervical afferents.9-11,16-18,21,22 Evident evidence using MRI showed that the vagus and cervical tract project to the parasial lobule, which is the genital region of the sensory cortex. This is consistent with the report that women with "complete" spinal cord injury at and above T10,4 who received deep brain stimulation demonstrated sexual attraction to the site of electrical stimulation. This observation suggested that the vagus nerves convey vagal and cervical afferent activity in the base, and was confirmed by MRI evidence that the NTS was activated by vagal and cervical stimulation in these women.13-15,19

Conclusion

We provide fMRI evidence that the vagus input to the brain is accessible non-invasively from the external ear, specifically the concha.

The pattern of activation and deactivation of brain regions in response to electrical stimulation of the concha provides a rational basis for the reported antiepileptic, antinociceptive, and antipsychotic effects of stimulation of the auricular branch of the vagus nerve.

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References