

# **Noninvasive Vagal Nerve Stimulation (nVNS) and the Trigeminal Autonomic Reflex: An fMRI Study**

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## **Objective:**

The aim of the study was to investigate the effect of noninvasive vagal nerve stimulation (nVNS) on the trigeminal autonomic reflex (TAR) with a new high resolution fMRI brain stem protocol.

**Background:** The TAR plays an important role in primary headache syndromes. The pathophysiology of the reflex itself is quite well understood. Recently we demonstrated that nVNS modulates the TAR. The mechanism for this modulation and which structures are involved is unknown.

## **Design/Methods:**

Twenty-one healthy participants (11 female, 10 male, mean age  $25.48 \pm 3.32$ ) were included into the study. Headache as well as psychiatric or neurological diseases were applied as exclusion criteria. The TAR was activated by stimulation of the nasal mucosa with kinetic oscillation stimulation (KOS) during the fMRI procedure, which leads to an increase in lacrimation.

A two-day within-subject design was used and the participants received either nVNS of the left cervical vagal nerve or sham stimulation of the left dorsal neck in a pseudorandomized order. In order to investigate the lower brain stem and medulla we used a specific segmentation routine and optimized the general linear model for the analysis of the fMRI data using the finite impulse response (FIR).

## **Results:**

The activation of the TAR prompted an increased BOLD signal of the right SII area and the bilateral insulae during intranasal stimulation. nVNS but not sham stimulation modulated the TAR and showed an inhibitory effect on specific brain stem networks.

**Conclusions:** nVNS had an inhibitory effect on the TAR and modulated brain stem processing of intranasal stimulation. These findings may help to explain the clinical effect of nVNS in cluster headache and migraine.