HIGH-RESOLUTION FMRI DETECTS ACTIVITY OF INDIVIDUAL BRAINSTEM NUCLEI DURING OPTICAL FLOW

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Purpose

A previous study (1) found that information-free electrical stimulation of the tongue, termed Cranial-Nerve Non-Invasive Neuromodulation (CN-NINM) produces sustained changes in neural processing when balance-impaired individuals view optic flow. Some of these changes were within the brainstem and cerebellum, however, the low-resolution of the collected images prevented precise localization of this effect. This study aimed to improve the localization ability by decreasing the voxel size of the fMRI imaging. Subjects DID NOT receive stimulation during the fMRI scans and any changes are therefore residual (not direct) effects of the stimulation.

Background

- Previous work has shown the feasibility of using the tongue as a route to deliver information-free electrical signals to the brain through the cranial nerves with efficient global innervation (1,2).
- A MRI study investigating psychological effects of this stimulation in individuals with balance dysfunction revealed sustained modulation of structures within the balance processing network including VS and the dorsal pons (1).
- The trigeminal and solitary nuclear complex is the gateway for the tongue sensations to the vestibular nuclei (Figure 1). Greater spatial detail is necessary to identify which, if any, of these nuclei are affected by the stimulation.

Methods

Subjects: Four women and two men (mean age 49.6±8.8 years) with various balance dysfunction etiologies, but common symptoms of deficits of balance, gait, and posture, underwent one week of therapy with CN-NINM. For detailed methods and stimulation procedures, please see (1). All subjects had a MRI scan on the day before the start of the therapy week and another MRI scan within three hours after completing the last therapy session.

Visual Stimulation: The vestibular system was stimulated with motion in the visual field (optical flow). Two visual stimuli were used (Figure 2). Subjects were shown visual stimuli for 12 seconds alternated with 6 seconds of fixation in a block-design paradigm. The order of the visual stimuli was pseudo-randomized.

Imaging Parameters: All MRI scans were collected on a clinical 3T GE 750 scanner (Figure 3). Functional images were collected with a 12°-weighted GE-EPI sequence (TR/TE = 2000/30, flip angle = 75°) to acquire BOLD signal in a 256 x 256 matrix over a 22 cm field of view and 23 axial slices (0.86 x 0.86 x 3.9 mm resolution). Visual stimuli were displayed on a computer screen at 800x600 resolution. Subjects DID NOT receive CN-NINM during the MRI scans.

Image Processing: All images were pre-processed with AFNI including slice-time and motion correction, low-pass filtering at 0.15 Hz, and spatial smoothing with a 3mm FWHM Gaussian. GLM estimation was performed using AFNI. All presented data is from an ANOVA investigating the effects of task (Static, Dynamic), time (Pre-CN-NINM, Post CN-NINM, and any interaction). The SUTT framework was used to normalize these structures into a restricted ICBM152 brain space at 1x1x2 mm resolution (4).

Results

- The effect of Task showed multiple activations that survived corrections for multiple comparisons (α < 0.001, volume > 14 voxels, Figure 4). These areas include the inferior olive bilaterally (MNI: X: ±4, Y: -31; Z: -45), the left vestibular nucleus (MNI: X: -7, Y: -38; Z: -41), the superior colliculus bilaterally (MNI: X: ±9; Y: -34; Z: -13), and the lateral geniculate nucleus of the thalamus bilaterally (MNI: X: ±8, Y: -29, Z: -3). There was also activation of the posterior vermis of the cerebellum (MNI: X: 0, Y: -73, Z: -29).
- There were no significant activations due to the effect of Time.
- The interaction of Task x Time showed activation of a region within the right dorsolateral pons (MNI: X: 10, Y: -35; Z: 38) and deactivation of the left cerebellar flocculus (MNI: X: -12; Y: -52, Z: -39).

Conclusions

- High-resolution fMRI can spatially localize brainstem activations better than standard MRM imaging.
- Optic flow activates structures involved in processing visual information, controlling eye movements, and interpreting information pertinent to balance.
- CN-NINM causes sustained changes within the trigeminal nucleus and flocculus that are task dependent. These changes may be related to the behavioral and subjective improvements due to CN-NINM (1).

Discussion

Effect of Task: Activations include structures known to be involved in processing visual stimuli and information relevant to balance. The vestibular nucleus receive input from the inner ear as well as descending projections from the cortex and cerebellum. The superior colliculus and lateral geniculate nucleus of the thalamus are both involved in the normal processing of visual stimuli and control of eye movement (including optic flow-induced nystagmus) (4).

Effect of Task x Time: Only two structures showed modified task activation due to CN-NINM. The flocculus of the cerebellum is known to be involved in balance processing and has reciprocal projections to the vestibular nuclei. The activation cluster within the pons appears to be the trigeminal nucleus – a structure not normally considered part of the balance-processing network, but which does receive afferent input from the tongue. Additionally, this structure has bidirectional connections to the vestibular nuclei (4.5). Modulation of this structure by CN-NINM stimulation supports the hypothesis that stimulation produces sustained plastic changes within the brainstem. These changes may be partially responsible for the improved behavioral and subjective results seen in subjects after stimulation (1).

References

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