Brain Injury and Mechanisms of Action of HBO2 for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (BIMA): Auditory Functional Magnetic Resonance Imaging at Baseline

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Target Audience Clinicians who study mild Traumatic Brain Injury in a clinical setting

Purpose: The purpose of this study was to evaluate auditory functional magnetic resonance imaging (fMRI) in military personnel with clinical mild Traumatic Brain Injury (mTBI) at the time of their baseline evaluation as part of a post-traumatic hyperbaric therapy program.[1] Auditory fMRI has previously been shown to provide evidence of brain injury as well as improvement following hyperbaric oxygen therapy.[2] We have observed a distinct pattern of altered fMRI signal in the auditory cortex and related regions on the side of the head associated with injury, which this study seeks to explore and quantify. Three methods were used for patient evaluation: clinical radiologist interpretation, computer analysis of the system vendor's fMRI analysis output, and a voxelwise General Linear Model (GLM) analysis.[3]

Methods A retrospective review of 70 subjects with clinical mTBI participating in a clinical trial[4] was conducted to assess potential auditory functional abnormalities. Auditory fMRI data were acquired using a 3T MR system (Achieva 3T; Philips Healthcare, Best, The Netherlands). Data were acquired using a standard single shot EPI sequence (FOV 240 mm, 44 slices acquired with a slice thickness/gap 3.0/0.5 mm, TR/TE 3000/35 ms) with a single block design with either 24 or 30 seconds "off " (eyes closed, no stimulation) followed by 24 or 30 seconds "on" (noun auditory stimuli) repeated five times for stimulation of right ear, left ear and bilateral simultaneous ears on each subject. The auditory cortex activation was assessed by 1) direct clinical radiologist interpretation, 2) computer analyzed objective quantification of the clinical data, and 3) full GLM-based computer analysis. Comparison between the radiologist interpretation and clinical computer analysis was conducted on a 5-point scale from no activity to mild increased activity. For the clinical computer analysis, the fMRI t-test activation likelihood analysis from the 3T MR system (iViewBOLD; Philips Healthcare) was automatically analyzed on a pixel-by-pixel basis using offline custom software to generate a quantitative scoring of right vs. left auditory cortex activation (Figure 1a). For the GLM analysis, image processing was performed using AFNI.[5] Right and left auditory cortex activations were measured by surviving voxel number (thresholded at beta-coefficient>0.7) within predefined cortical regions (Figure 1b). The number of GLM activation voxels was then correlated with the corresponding clinical computational analysis results. Eleven subjects with incomplete image processing were partially or completely excluded from correlation analysis.

Results Of the 70 subjects reviewed, 55 successfully completed the auditory fMRI evaluations. Based on the fMRI studies, 27 of the 55 were classified as normal (17, 31%) or low-normal 10, 18%). Fifteen (27%) of the 55 were classified with a central auditory processing abnormality whereby right or left ear responses were significantly abnormal with the bilateral stimulation similar to the abnormal ear response. Seven (13%) were classified with a probable unilateral hearing deficit and/or central auditory processing abnormality whereby right or left ear responses were significantly abnormal with the bilateral stimulation similar to the normal ear response. In 3 (5%) of the subjects the bilateral response was significantly greater than the right or left alone, and in 3 (5%) of the subjects the bilateral response was significantly less than the right or left alone. Comparison between the clinical and computer analysis methods resulted in 67% concordance (identical), 32% near-concordance (one level difference), and 1% discordant. Comparison between the clinical computer and GLM analysis yielded significant correlations in right and left ear responses (p<0.05) for the full subject group (Table 1).

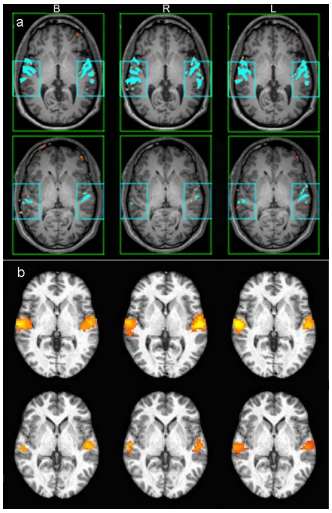

Figure 1. a) Clinical computational and b) GLM-derived activation maps of bilateral, right, and left ear stimulation in mTBI subjects classified as "normal" (clinical score=4) and "moderately decreased" (score = 2) by both clinical computational and qualitative evaluation.

	Bilateral Ear Stim (n=60)	Left Ear Stim (n=61)	Right Ear Stim (n=60)
Left Auditory Cortex	r=0.519; p<0.00001	r=0.403; p<0.01	r=0.552; p<0.00001
Right Auditory Cortex	r=0.545; p<0.00001	r=0.421; p<0.001	r=0.267; p<0.05

Table 1. Correlation coefficients and corresponding p-values for clinical computer and GLM analysis comparison.

Discussion/Conclusion: The results of our study show that, based on the significant correlations of the right and left ear responses from the three different assessment methods evaluated, auditory fMRI provides a reliable and reproducible method for evaluating potential auditory dysfunction in military personnel with clinical mild traumatic brain injury (mTBI). There is a high degree of concordance between clinical evaluations and a computer analysis of the clinical data; moreover, computer analysis of the clinical data demonstrates high correlation with GLM analysis.

References

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