

## PROJECT SUMMARY (See instructions):

Despite the incidence of spasticity in post-stroke survivors and the significant challenge that it poses for patient care, the pathophysiology of post-stroke spasticity remains poorly understood. Although accumulated evidence supports the supraspinal origins of spasticity, it is currently not possible to distinguish between two potentially contrasting theories, one supporting the dominant root cause being in the lateral vestibular nuclei (LVN) and their descending pathways (vestibulospinal), and the other emphasizing the contribution of the reticular nuclei (RN) and their own descending pathways (reticulospinal tract). In an effort to resolve this debate, we aim to measure in vivo activity of the brainstem in patients with post-stroke spasticity. One recent method of delineating the origins of spasticity is through auditory stimulation, which supposedly activates the LVN by stimulating the sternocleidomastoid muscles. However detractors believe this may simply be a startle reflex acting through the RN. Our first aim is a pilot study to precisely identify the neural correlates of auditory stimulation on both healthy individuals and stroke patients via fMRI of the brainstem. Yet the direct connection to spasticity is still difficult to make, and as a result, our next aim is to use robotic perturbations to elicit a spastic response during brainstem functional imaging. We have developed our own MR-compatible robotic manipulator capable of flexion/extension of the wrist at speeds that can induce spastic responses. Our goal in this project is to validate this robotic perturbator on healthy individuals and obtain pilot data for this experiment in stroke patients. This will be the first neuroimaging data collected of the brainstem during a spastic response and will unveil a new paradigm for neuroscientific investigation in stroke.

## RELEVANCE (See instructions):

This project aggregates a multidisciplinary team of researchers to formulate novel technologies and methodologies to investigate brain pathophysiology, fully in the spirit of UT BRAIN. The contact PI, Dr. James Sulzer, Ph.D. (UT Austin), specializes in fMRI, and brainstem-based online neurofeedback using fMRI and development of MR compatible robotics, and will be in charge of data analysis. Dr. Fabrizio Sergi, Ph.D. (Rice University), is the developer of the MR-SoftWrist, a MR-compatible wrist perturbator, and will contribute to the phase of experimental testing involving the robot. Dr. Sheng Li, M.D. Ph.D. (UT Health Sciences Center, Houston) specializes in stroke rehabilitation with a specific expertise in spasticity, and will be in charge of clinical evaluations. Dr. David Ress, Ph.D. (Baylor College of Medicine) is a world-renowned expert in brainstem imaging with fMRI. This will be the first collaboration between any of these researchers. The proposed research extends into novel directions: to localize the responses of deep brainstem nuclei to auditory stimuli, and to directly measure correlates of a spastic response in the brainstem.