

## **Cortical dynamics of the speech motor control network in the non-fluent variant of Primary Progressive Aphasia**

Hardik Kothare, Kamalini Ranasinghe, Leighton Hinkley, Danielle Mizuiri, Michael Lauricella, Susanne Honma, Valentina Borghesani, Corby Dale, Wendy Shwe, Ariane Welch, Zachary Miller, Maria Luisa Gorno-Tempini, John Houde, Srikantan Nagarajan

Primary Progressive Aphasia (PPA) is a clinical syndrome in which patients progressively lose speech and language abilities. The nonfluent variant of PPA (nfvPPA) is characterised by impaired motor speech and agrammatism. These speech and language deficits are often associated with left fronto-insular-striatal atrophy in nfvPPA patients. Functional magnetic resonance imaging as well as diffusion tensor imaging studies further suggest impaired connectivity of neural circuitry involved in speech motor control. However, none of these studies provide sufficient temporal resolution to document the dynamics of the recruitment of the speech motor control network during vocal production.

In this study, we employed magnetoencephalographic (MEG) imaging to investigate sensorimotor integration during an altered auditory feedback paradigm in 18 nfvPPA patients and 17 healthy controls. Participants were prompted to phonate the vowel /a/ for ~2.4s. Unbeknownst to them, following a randomly jittered delay of 200 to 500 ms after voice onset, the pitch of their feedback was shifted either up or down by 100 cents (1/12th of an octave) for a period of 400ms. Vocal pitch responses were examined as the participants responded to this pitch perturbation. Task-induced neural oscillations relative to a pre-perturbation baseline were examined in the theta-alpha (4-13 Hz) and the beta bands (13-30 Hz) associated with attention and sensorimotor integration respectively. Nonparametric statistical tests were performed to look at neural activity differences in patients compared to healthy controls with cluster-threshold corrections for multiple comparisons.

Behaviourally, nfvPPA patients showed a smaller compensation response to pitch perturbation than controls. Baseline pre-perturbation pitch variability did not differ significantly between the two groups, indicating that reduced vocal compensation cannot simply be attributed to insufficient vocal control range in patients. Patients also exhibited reduced task-induced theta-alpha neural activity in the right superior temporal gyrus, right superior temporal sulcus, right middle temporal gyrus and the right temporoparietal junction. Patients also showed increased task-induced beta-band activity in the left dorsal sensorimotor cortex, left premotor cortex and the left supplementary motor area.

Collectively, these results suggest significant impairments in processing of auditory feedback during vocal production in nfvPPA patients.