## The Neural Circuitry Underlying the "Rhythm Effect" in Stuttering

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Developmental stuttering is a communication disorder characterized by impairments in the ability to produce smooth and timely articulations of planned utterances. Stuttering disfluencies are reduced, however, when speakers synchronize their speech movements with a steady beat ("rhythm effect")[e.g., 1]. It is well-documented that stuttering is associated with disruptions in the cortico-basal ganglia motor loop [2], and it has been proposed that this system is involved in self-generated ("internal") timing cues [3]. The rhythm effect may improve fluency by bypassing the impaired internal timing system and recruiting the intact "external" system, comprised of the lateral premotor cortex and cerebellum. To determine whether this is the case, we used functional magnetic resonance imaging (fMRI) to investigate brain activation and functional connectivity during normal and rhythmic speech production in both adults who stutter (AWS) and adults who do not stutter (ANS).

During a sparse-sampled functional MRI session, 17 AWS and 17 ANS read short sentences aloud. Before each trial, participants heard a series of eight isochronous tones. In the 'rhythmic' condition, they were cued to produce the sentence at the same speed as the tones. aligning each syllable to a beat. In the 'non-rhythmic' condition, they were cued to ignore the tones and read the sentence using natural stress and pacing. Trials were randomly ordered and interspersed with a silent baseline where participants heard the tones but did not speak. All speech productions were analyzed offline to extract speech rate, rhythmicity, and number of disfluent trials. Each participant's functional data were motion corrected and coregistered to a highresolution T1-weighted structural image. Mean activation for each trial was estimated within anatomical regions-of-interest (ROIs); cortical ROIs were labeled with a system tailored for studies of speech [4] and subcortical and cerebellar ROIs were derived from probabilistic atlases. Comparisons of mean activation between groups and conditions were evaluated with a false discovery rate (FDR) correction to account for multiple comparisons. ROI-to-voxel functional connectivity was also calculated for each subject in each condition and comparisons across tasks and groups were made using a generalized psychophysiological interaction (gPPI) analysis [5]. A Bonferroni correction was applied to significant clusters to account for the large number of ROI seeds.

Behaviorally, AWS produced fewer disfluent trials in the rhythmic condition than in the non-rhythmic condition (p = 0.023). Imaging results indicated that ANS had greater activation in rhythmic compared to non-rhythmic conditions in cortical areas associated with speech planning, auditory feedback control, and timing perception (left planum temporale, left supplementary and pre-supplementary motor area, left superior parietal lobule, left anterior insula, right ventral premotor cortex, left planum polare, and left ventral anterior thalamus). AWS demonstrated similar trends, however, no ROIs were significant after FDR correction. Further examination indicated there were no significant differences between the AWS and ANS group.

The ROI-to-voxel functional connectivity analysis showed that only AWS, not ANS, had increased functional connectivity between bilateral cerebellum lobule VIIIa and bilateral

orbitofrontal cortex (OFC) as well as increased connectivity among cerebellar regions during rhythmic speech as compared to non-rhythmic speech. In addition, there was a group by condition interaction in the connectivity between left ventral premotor cortex and right inferior cerebellum where AWS had increased connectivity during the rhythmic condition, while ANS had decreased connectivity. The opposite effect was found between cerebellum lobule V and left medial sensorimotor cortex extending into the left supplementary motor area.

The rhythmic speaking condition thus led to an increase in fluency for AWS along with increases in functional coupling between inferior cerebellar regions and OFC in AWS. This result aligns well with previous studies that associate 1) successful compensation for stuttering symptoms with activation changes in these regions [7,8] and 2) reduced stuttering symptoms with greater connectivity between these two regions during rest [8]. Together, these findings suggest that changes in activation and connectivity between the cerebellum and OFC are a common feature of natural, therapeutic, and rhythmic fluency enhancement in AWS.

In addition, increased connectivity between the cerebellum and left lateral premotor cortex during rhythmic speech indicates greater functional coupling within the "external" timing system in AWS. Decreased connectivity between the cerebellum and left medial premotor cortex further suggests that the two timing systems decouple in this condition in AWS. Overall, this study supports the idea that speaking with an external pacing stimulus improves fluency in AWS by recruiting the intact external timing system and bypassing the impaired internal timing system.

## References

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