Measuring the functional effects of BOTOX on the brainstem using MR Spectroscopy (MRS) and fMRI

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STATISTICAL ANALYSIS PLAN

MRS Data Analyses

Metabolite FIDs will be averaged within each task and processed using TARQUIN (v.4.3.6) software for spectral fitting. We chose a block design (vs. event-related) for its higher detection efficiency (at the cost of the inability to sort by individual trial performance or estimate HRF shape)[75]. Within-task dynamics will be investigated by a moving average windowing approach. The minimum temporal window will be determined by the SNR. The corresponding binned water unsuppressed spectra will be used as an internal reference for each condition. The acquired MRS spectra will be corrected for tissue type and T2 relaxation differences. Additionally, using TARQUIN we will obtain values for all metabolites mentioned in Preliminary results. These values will be collected to ensure that the changes in Glu and GABA signals are real and not due to a result of some other general effect on the MRS data (e.g., BOLD related change in signal). The water peak amplitude changes will be processed with a custom designed MATLAB script[5].

Functional MRI Data Analyses

The **functional MRI data** will be pre-processed and analyzed using AFNI (Cox, 1996; afni.nimh.nih.gov) and in-house programs written in Matlab and Python. The fMRI data were first subjected to a traditional general linear model analysis using multiple regression in AFNI (Cox, 1996). The task vectors of interest will be individually modelled for each participant's functional data utilizing a deconvolution approach built into AFNI's 3dDeconvolve (Ward, 2001). 15 tent functions will be used to estimate the hemodynamic response to each condition. The resultant fit coefficients (β coefficients) represent activity versus baseline for each condition of interest at a given time point in each voxel. The sum of the resultant fit coefficients over the bulk of the expected hemodynamic response (3-13.5 seconds after trial onset) will be taken as the model's estimate of the response for each trial type and passed on to group-level analyses. The hypotheses will be primarily tested using the standard linear model. Brain activity for positive and negative emotions pre- and post-BOTOX injection will be compared in a 2x2 ANOVA, with planned comparisons for follow-up.

Resting state data will be detrended using 2nd order Legendre polynomials. The time series will be normalized to have zero mean and unit variance and the motion vectors and first derivatives will be regressed out of the signal. The first 6 principal components of the variance will be computed using CompCor (not including global signal) and regressed out of the signal (Behzadi et al., 2007). The data were then temporally bandpass filtered (0.009 to 0.08 Hz) and TRs with framewise displacement >0.5mm, as well as those one TR before and two TRs after, will be removed.

Structural brain volumes will be calculated on the MP-RAGE for each participant using Freesurfer's automatic software for volumetric measures (FreeSurfer 2016; Fischl et al. 2002). These volumes will then be normalized by dividing by total intracranial volume for each participant. T-tests for pre- vs. post- BOTOX injections can then be examined.