Mapping the neural circuitry of antisaccade performance using DTI

D. S. Tuch[1], G. A. Ketwaroo[2], M. S. Cain[3], C. L. Sauder[1], K. N. Thakkar[1], F. E. Polli[1,4], J. J. Barton[5], D. S. Manoach[1,6]

[1]Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, United States, [2]Harvard Medical School, Boston, MA, United States, [3]Department of Psychology, University of Califorina, Berkeley, Berkeley, CA, United States, [4]Department of Psychiatry, Suffolk University, Boston, MA, United States, [5]Neuro-ophthalmology Section, University of British Columbia, Vancouver, British Columbia, Canada, [6]Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States

Background – The antisaccade (AS) task (1) provides an excellent model to investigate executive control over reflexive behavior. In the AS task, the participant is asked to suppress the reflexive urge to look at a target that appears suddenly in the peripheral visual field, and instead look away from the target. The suppression of the reflexive prosaccade (PS) makes the AS task a powerful tool for studying top-down inhibition of automatic, reflexive behavior. Despite the extensive use of the AS task in clinical and cognitive neuroscience (2,3), the neurophysiological mechanisms which underlie interindividual variations in AS performance remain largely unknown. Here we sought to test whether AS performance in young healthy adults is correlated with diffusion tensor fractional anisotropy (FA), a putative marker of white matter (WM) microstructural integrity. We found a high correlation between AS performance and FA in precentral gyrus WM, intraparietal WM, cerebellum, and substantia nigra. The localization of the AS-FA correlation to these specific regions is consistent with previous functional neuroimaging, animal neurophysiology, and lesion studies (2) which have identified these areas as key nodes in the AS network.

Methods, MRI – Single-shot EPI DTI was acquired on 8 young healthy participants (age=22.1±2.3 years) on a 3T Siemens Trio MRI with TR/TE=8400/82ms, b=700s/mm^2, 60 diffusion directions, 10 T2 images, 2 mm resolution, 64 oblique (AC-PC) slices. Each participant's FA volume was normalized to MNI space using the FSL FLIRT tool (4), and then smoothed (6mm FWHM, 6mm extent). **EEG/MEG/EOG** – MEG data were recorded from all participants using a 306-channel dc-SQUID Neuromag Vectorview system recording at a 600Hz sampling rate. Twelve channels of EEG data were collected using non-magnetic EEG scalp electrodes embedded in an electro-cap. Two bipolar pairs of EOG electrodes captured vertical and horizontal eye movements and blinks. **Saccade Task –** The participants performed the saccade task in the MEG. The task consisted of a random sequence of PS and AS trials. Each trial consisted of prompt (300ms) - fixation (1700ms) – target (1000ms) – fixation (1000ms) (Fig. 1). EOG saccadic data were manually scored to eliminate incorrect trials and trials corrupted by eye blinks. Correct saccades were used to compute mean PS and AS latencies. **Analysis** – To partial out the effect of PS latencies, the AS latencies were orthogonalized with respect to the PS latencies. For each voxel in template space, a linear model FA=$\beta_0+\beta_a\times t_a$ was fit to the data, where FA is the participants' FA values for that voxel, t_a is the orthogonalized AS latencies, and β_0, β_a are the model regression coefficients. The linear model was also computed for the unorthogonalized PS and AS latencies.

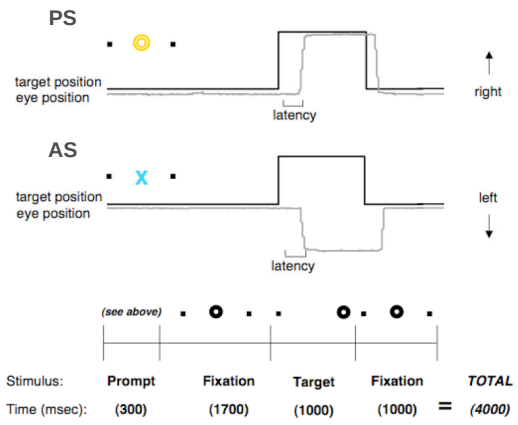

Fig. 1. Saccade paradigm. 300ms prompt is presented instructing the participant to perform either a PS (yellow circle) or AS (green X). After fixation, the target reappears at a random side and the participant performs the appropriate saccade. The trial repeats after 1000ms fixation.

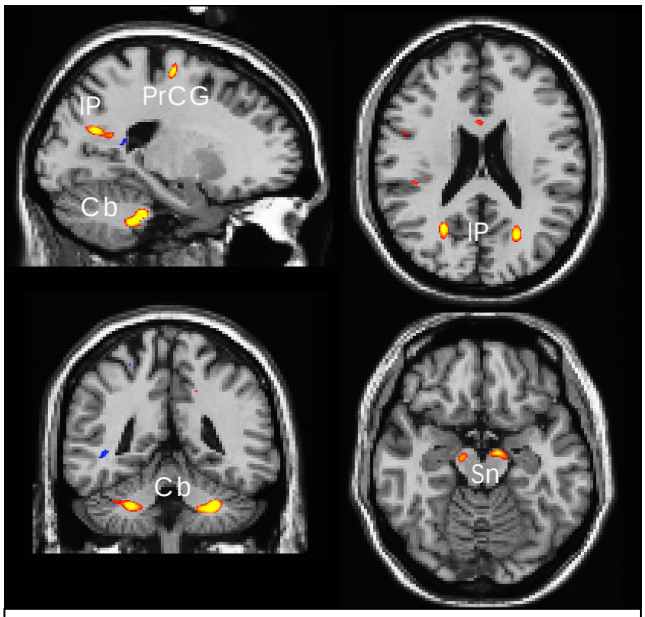

Fig. 2. Group regression coefficient (β_a) for orthogonalized AS.

Results – The group regression coefficient (β_a) for orthogonalized AS latency localized to precentral gyrus (PrCG) WM (homologue to monkey frontal eye field (FEF), intraparietal WM (IP) (homologue to monkey lateral intraparietal area (LIP)), cerebellum (Cb), and substantia nigra (Sn) (2) (Fig. 2). The correlation coefficient for the unorthogonalized PS and AS latencies both localized the frontostriatal pathway from dorso- lateral prefrontal cortex (dlPFC) to the midbody of the caudate nucleus (CD) (Fig.3).

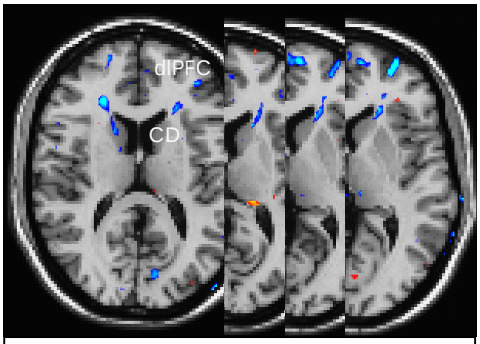

Fig. 3. Ccorrelation coefficient map for unorthogonalized AS latency shows the frontostriatal pathway from dlPFC to CD.

Conclusions – AS latency and FA were found to be correlated in specific anatomic areas consistent with the established functional neuroanatomy of the AS task (2). The frontostriatal pathway from dlPFC to CD (Fig. 3) is consistent with the role of frontal inhibition of the basal ganglia in PS and AS performance (5). The physiological mechanisms underlying the AS-FA correlation are not yet clear, but may be the contribution of myelin, axon diameter, and histoarchitecture to both FA and conduction velocity. Future work will investigate the correlation between FA and the E/MEG cortical source latencies for the AS task.

References – 1. Hallett PE. *Vision Res*. **18**, 1279-96, 1978. 2. Munoz DP, Everling S. *Nat Rev Neurosci*. **5**:218-28, 2004. 3. Everling S, Fischer B. *Neuropsychologia*. **36**:885-99, 1998. 4. Jenkinson M. et al. *Neuroimage*. **17**, 825-41, 2002. 5. Hikosaka O. et al. *Physiol Rev*. **80**:953-78, 2000. **Acknowledgments** – Supported in part by Glaxo Smith Kline, NIMH 067720, NCRR RR14075, the Athinoula A. Martinos Foundation, and the MIND Institute.