Imaging oculomotor subsystems in the cerebellum at 7 Tesla

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Introduction Many new acquisition techniques and coil systems are being developed to take advantage of the increased power and accuracy available when imaging at high fields. BOLD specificity and contrast to noise is enhanced at high fields allowing the delineation of neuronal activity in the human cortex at a finer scale than previously possible (1-3), and this is highly valuable when imaging anatomically complex structures with small nuclei and/or complex cytoarchitechtonics such as the cerebellum (Cb) (4).Common challenges, including RF-tissue interaction, local inhomogeneities from susceptibility transitions, such as the ear canal, physical location with respect to receivers and anatomical complexity (i.e. small microvasculature and deep nuclei) must be considered in order to reduce signal dropout particularly for Cb. This study was undertaken to prove efficacy of combinatorial methods which overcome these challenges while simultaneously leaving enough space within the transmit coil to monitor the eyes. The end goal was to successfully image Cb in order to further investigate the involvement of this structure in oculomotor processes using eye tracking. This research benefits investigations on the role of the Cb in motor and cognitive systems under both normal and adaptive situations.

Methods Four subjects were scanned at 7T (Philips) using two high-density 16-channel surface coils ((3), MR coils BV; 32 channels total) and a volume transmit coil (Nova Medical, MA) with dual transmission for excitation. The coils were placed at the back of the head at the level of the Cb using the inion as a landmark. B0 and B1 fields were shimmed separately on the Cb using in-house tools. fMRI data were acquired using a segmented 3D-EPI (TR/TE:42/25ms, flip: 20deg, EPI factor: 29, voxel size: 1.25mm isotropic, FOV: 140x160x50, 40 coronal slices, volume acquisition time: ~3s). Anatomical data were also acquired: T1w MPRAGE (TR/TE: 8.0/3.1ms, FOV:140x160x50, flip:10deg,voxel size: 0.63 mm isotropic), T2*w 3DEPI (TR/TE: 70/27ms, EPI factor: 13, FOV:140x160x40, flip:20deg, voxel size: 0.5 mm isotropic). Classic cued pro-/anti-saccade, saccade adaptation (driven by unseen displacement of the saccade endpoint), and finger (thumb) movement tasks were used elucidate Cb activations, in a 20s on/off block design. Pro- and anti-saccades were mixed within a 20s block, followed by 20s of fixation at a central fixation cross. Visually cued thumb movement was at a rate of 2 Hz. One ~8 min run was performed per task. Eye movements were recorded by a monocular infra-red video-based eye tracking system at a sampling rate of 60 Hz (ViewPoint EyeTracker, Arrington Research, Scottsdale, USA), adapted for use at 7T by NordicNeuroLab (Bergen, Norway). The eyetracker was attached on the transmit coil; two infra-red LEDs on either side of the camera were aimed at the subject's eye. The left eye was monitored to provide behavioural feedback controlling stimulus timing and to measure the changes in saccade amplitude as the oculomotor plan changes in response to saccadic displacement. Every run started with a 16-point calibration routine.

Results Figure 1 shows that oculomotor areas of Cb, namely oculomotor vermis (Ic and II), are responsive during both eye movement tasks; and that CrusII is responsive when the task requires an eye movement that differs from the visual motor plan. For pro-and anti-saccades (contrasting both saccade types versus rest) both CrusI and CrusII were activated and activation in these areas is differentiated during saccade adaptation with significant differences in beta values only at the start of adaptation and none at the end. In addition, the location of activations for different types of movement is highly separable in all subjects, i.e. for eye versus finger movements (Figure 2), and for different types of cognitive tasks, i.e. consciously reflexive versus volitional in pro/anti and unconscious adaptation.

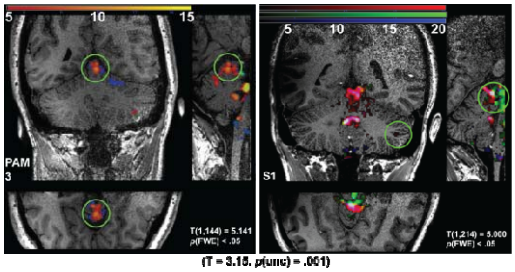

Figure 1. Oculomotor activations in Cb. *Left*: oculomotor vermis (vIc and vII, circled) and CrusII for pro/anti saccades. *Right*: Contrasting baseline saccades with advancing stages of oculomotor learning reveals graded responses; CrusI/II and oculomotor vermis respond strongly to mismatched visuomotor predictions (red) at the onset of learning; activity in vIc (green) is seen only when saccade amplitudes differ from visually expected amplitudes and vermal activity is very low by the end of the learning (blue). Colours of overlapping activations are additive.

Discussion With the present setup, BOLD signal changes in Cb resulting from motor activity in runs lasting less than ten minutes were strong enough to pinpoint activations very accurately within each individual: oculomotor vermis and crus II for saccades, and ipsilateral V-VI for finger movement. This spatial accuracy decreases the need to combine acquisitions from multiple subjects to find functional regions of interest, and together with the decreased acquisition time allows for a larger number of investigations within one individual or a small group. Additionally, this arrangement allows for favourable signal reception from the cerebellum, and leaves ample space within the transmit coil enabling additional monitoring equipment such as an eye tracker.

Our initial results also hold implications for motor-learning research in humans as well as for modelling these systems. Oculomotor regions of Cb activate differently in the context of expected versus unexpected outcomes. Increasing BOLD signal changes were related to task difficulty with regard to outcome expectations of the motor system in response to visual inputs. This could relate to activity-dependent representations of the presence or absence of a motor error within the regions already known to be associated with eye movements, possibly akin to animal-based findings relating increased complex spiking of purkinje cells with motor learning (5). Further research is warranted to extend these results.

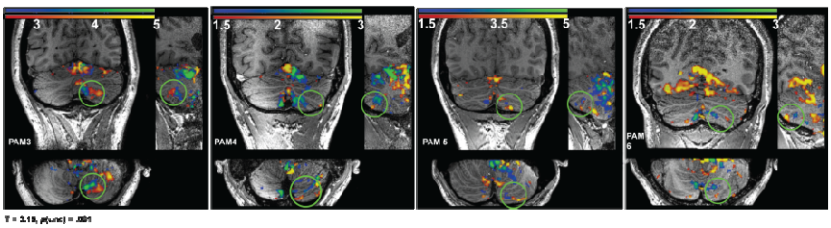

Figure 2. Dissociable motor-related activity in lobules HVIIb/HVIII reproducible in each subject despite large intersubject variability in Cb structure. Finger motion in blue-green, saccades in red-yellow.

References (1) Shmuel et al, *NeuroImage* 35: 539–552, 2007. (2) Yacoub et al. *NeuroImage* 37: 1161–1177, 2007 (3) Petridou et al, *NMR Biomed* 26(1): 65-73, 2013, (4) van der Zwaag et al, *NeuroImage* 67(C): 1–9, 2013, (5) Soetedio & Fuchs, *J Neurosci* 26(29): 7741-55, 2006.