Laminar-specific fingerprints of different sensorimotor areas obtained during imagined and actual finger tapping

Robert Trampel[1], Pierre-Louis Bazin[1], Andreas Schäfer[1], Robin Martin Heidemann[1], Dimo Ivanov[1], Gabriele Lohmann[1], Stefan Geyer[1], and Robert Turner[1]
[1]*Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany*

Introduction: The response of the cerebral vascular system, and hence the BOLD signal, depends both on the specific task and the cortical area involved [1,2]. Here we consider the sensorimotor system during planning and execution of motor tasks [3,4]. Functional MRI at 7 Tesla now provides sub-millimeter resolution, and thus can resolve BOLD responses at different cortical depths in human brain [5-7]. Whether such observations can discriminate the layer dependence of the underlying neural activity, however, remains debatable [8]. Because blood oxygenation changes are maximal at the cortical surface, BOLD signal changes are also greatest there, decreasing with cortical depth. Within the cortex, the principal intracortical veins perpendicular to the pial surface (penetrating veins) effectively integrate the oxygenation changes taking place at the deeper levels which they drain. Despite this surface bias and the smoothing effect, however, it may still remain possible to detect subtle activation differences between cortical layers within a specific area, when it is activated by different experimental conditions. Differences in layer dependence of the BOLD time course may also be observable across different cortical areas involved in processing the same task. Several different cortical areas within the sensorimotor system are activated during imagined and executed finger tapping [9-11]. This provides an elegant paradigm for investigating the capacity of sub-millimeter fMRI at 7 Tesla to discriminate cortical depth-dependent BOLD time courses, thus enabling a detailed functional fingerprint of the sensorimotor system.

Method: All experiments were performed on a 7 T whole-body MR scanner (MAGNETOM 7T, Siemens Healthcare, Erlangen, Germany) using a 24 channel phased array coil (Nova Medical Inc, Wilmington MA, USA). The study was carried out with ethical approval from the local university and informed consent was obtained. In order to identify the M1/S1 area, a whole-brain T1 map was acquired prior to the functional experiment. For fMRI, 26 axial EPI slices were acquired at the position of the "hand knob". In order to achieve an isotropic resolution of $(0.75\ \text{mm})^3$ a zooming technique was utilized [12]. The other sequence parameters were: TR = 3.3 s; TE = 25 ms; FA = 80°. For the fMRI experiment a stimulus paradigm consisting of 4 conditions was used: no finger movement (rest); no finger movement but imagining finger movement (imagining); "classical" finger tapping (tapping); movement of the fingers without touching the finger tips (moving). Each block consisted of 8 TR's and was repeated 15 times, respectively, resulting in 480 time steps. LIPSIA was used for data analysis [13] in combination with a de-noising approach [14]. No spatial smoothing was applied. The activation maps were corrected for multiple comparisons using FDR with $p < 0.05$. For cortical depth-dependent analysis, the cortex was segmented and automatically contoured into 4 laminae ('deep layer' adjacent to white matter; 'middle layer 1'; 'middle layer 2'; 'superficial layer' adjacent to CSF) using MIPAV [15]. The corresponding BOLD signal time courses were separately extracted for voxels within each lamina and the mean signal difference compared to the rest condition was calculated. Finally, the cortex was manually parcellated into 4 approximate anatomical areas, corresponding to primary motor cortex (Brodmann Area BA4), primary somatosensory cortex (BA3), premotor cortex (BA6) and posterior somatosensory cortex (BA2). The activation maps obtained and the "hand knob" were used as guidance. Figure 1 shows a T1 map with the 4 cortical regions analyzed (BA6 in black; BA4 in pink; BA3 in yellow; BA2 in orange).

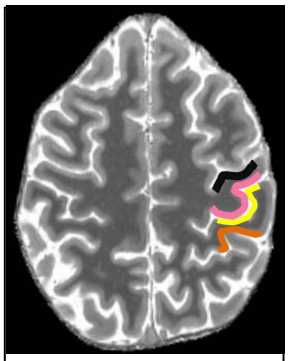

Fig. 1. T1 map showing ROIs.

Results: Figure 2 shows the time courses of a single subject, collapsed over one task cycle, of the mean BOLD signal in each lamina in each of the cortical regions depicted. The typical signal gradient from the pial surface towards white matter is obvious. However, significant differences can also be detected by comparing different conditions (e.g., tapping and moving in the somatosensory cortex), different cortical regions (e.g., primary motor cortex and primary somatosensory cortex during tapping) and, most interestingly, by comparing the signal ratios between different layers either in distinct cortical regions or during different conditions.

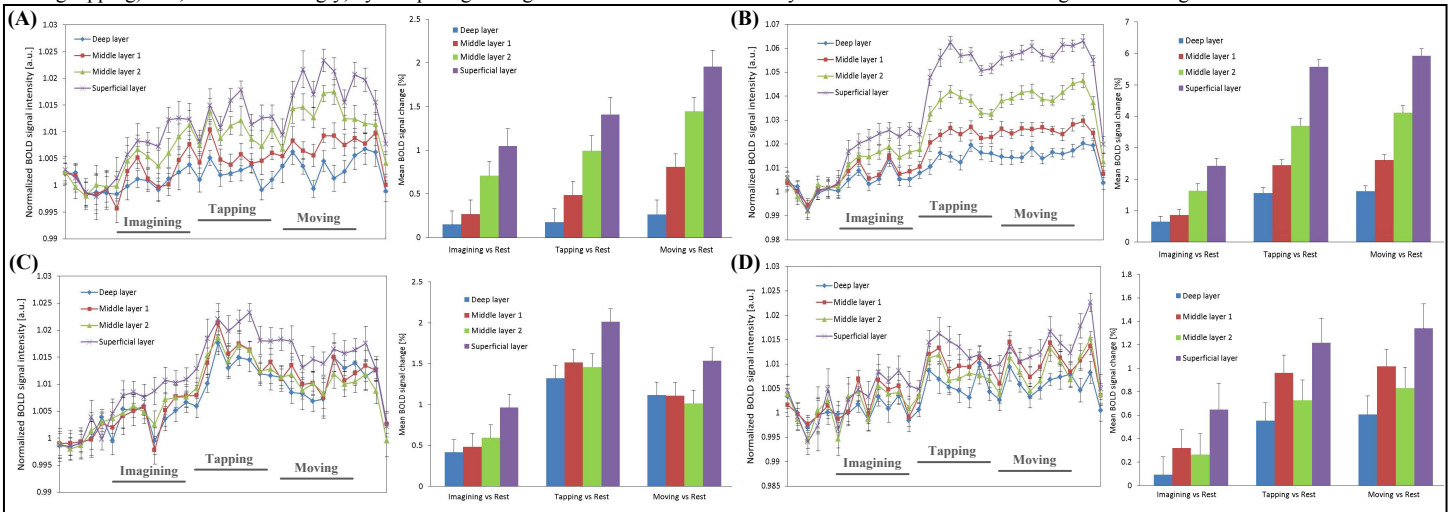

Fig. 2. Time courses and mean BOLD signal in **(A)**: Premotor cortex BA6 (marked black in Fig. 1); **(B)**: Primary motor cortex BA4 (pink in Fig. 1); **(C)**: Primary somatosensory cortex BA3 (yellow in Fig. 1); **(D)**: Posterior somatosensory cortex BA2 (orange in Fig. 1).

Discussion and Conclusion: The study demonstrates the feasibility of observing cortical depth-dependent differences which are normally buried under the BOLD signal gradient associated with the vascular anatomy of the cortex. The SNR required to perform fMRI at the required resolution was provided by the high magnetic field strength of 7 T and the use of a high quality phased-array RF receive coil. By comparing the BOLD signal at cortical depths corresponding to input or output layers, our approach may assist in the assignment of neural causality. In this study the output layer of primary motor cortex (cortical layer V) corresponds roughly to 'middle layer 1' (depicted in red in Fig. 2). In primary motor cortex, for example, this layer appears to be relatively less activated, compared with the corresponding 'deep layer' (depicted in blue in Fig. 2) and with the corresponding 'superficial layer' (depicted in purple in Fig.2), during imagery than during tapping or moving (see Fig. 2B). This could reflect differences in output activity between motor imagery and actual performance.

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