Science Advances
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Supplementary Materials for

Layer-specific activation of sensory input and predictive feedback in the human primary somatosensory cortex

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Published 15 May 2019, *Sci. Adv.* **5**, eaav9053 (2019)
DOI: 10.1126/sciadv.aav9053

This PDF file includes:

Supplementary Materials

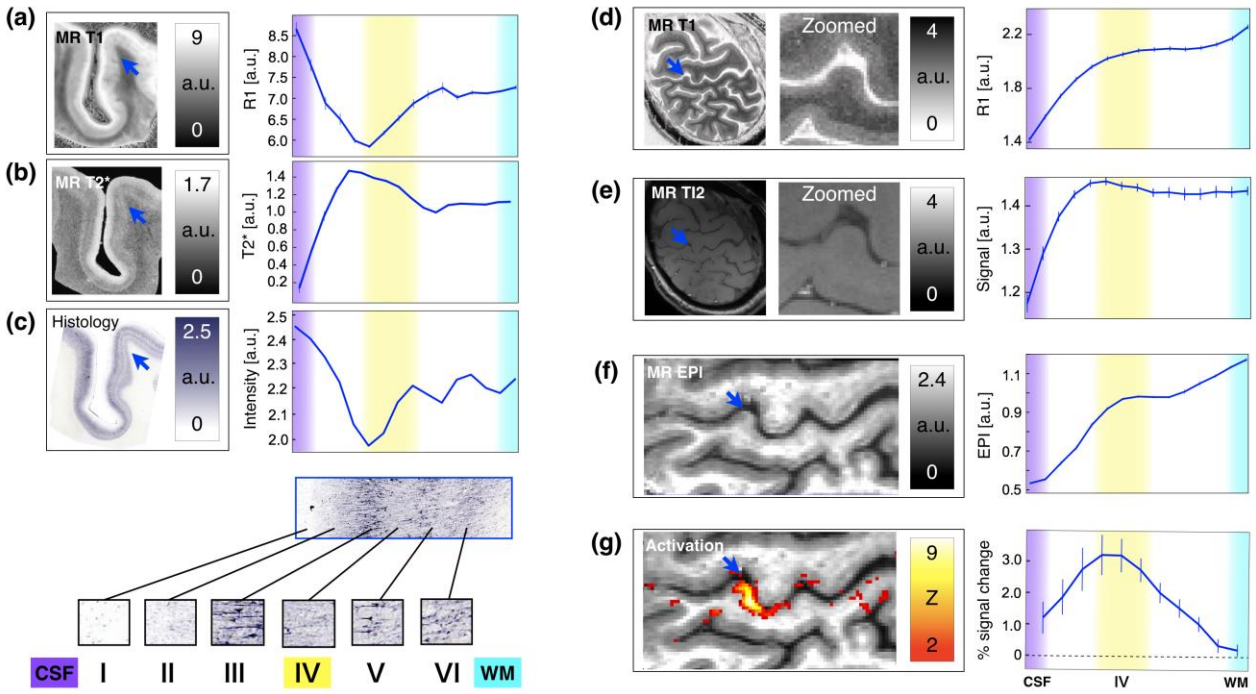

Fig. S1. Assignment of functional layer fMRI activity to the location of cytoarchitectonically defined cortical layers by comparison between high-resolution postmortem and in vivo data. Panels (a) to (b) refer to 200 µm post-mortem data identifying MR-sensitive layer-landmarks. Panel (c) depicts SMI311 histological staining results of the same part of the cadaver brain sample. It can be seen that deep layer III comes along with a peak in T1 and T2*-values. Indication of the landmarks from the ex-vivo data are also visible in in-vivo data of participants of this study (d) to (g) and are used to assign the position of layers across functional profiles.

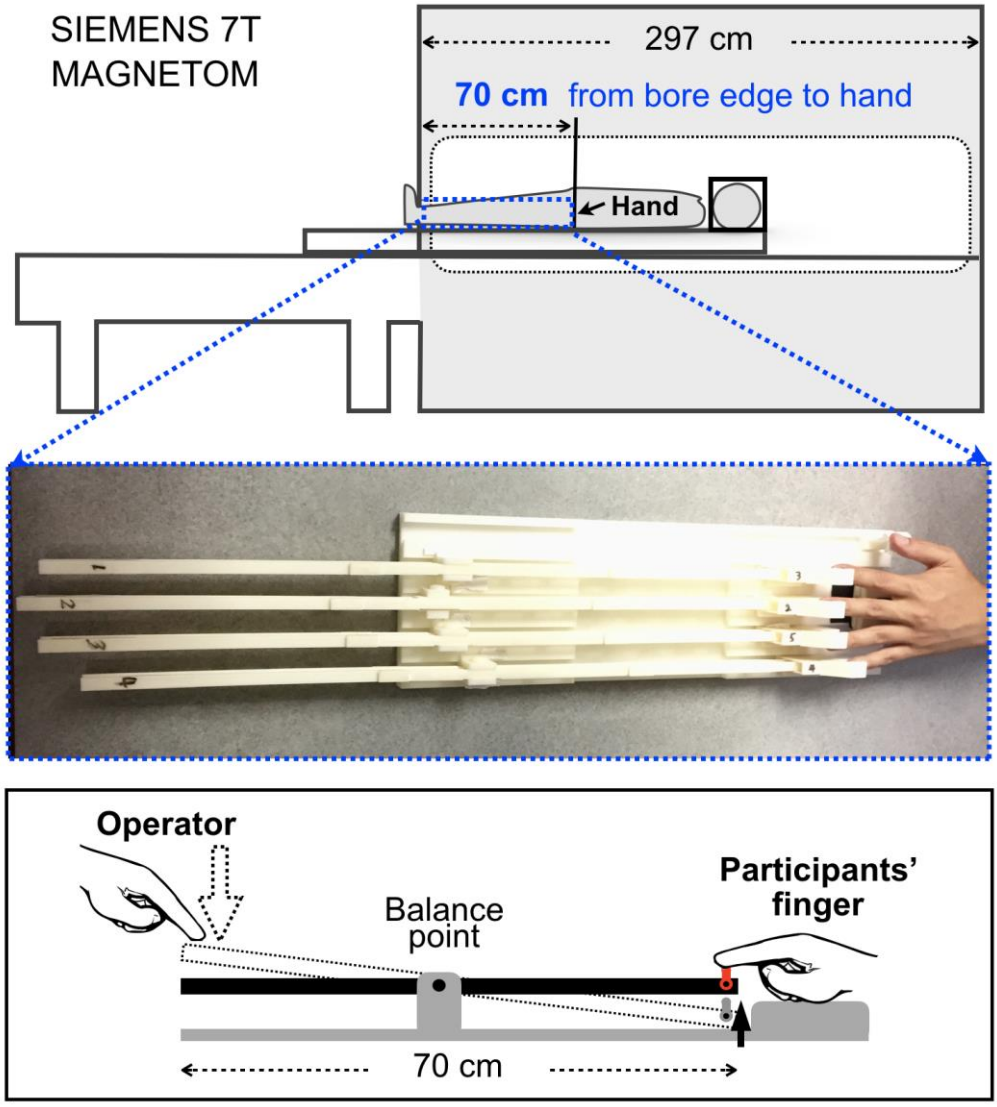

Fig. S2. Custom-designed, metal-free, 3D-printed finger stimulation device. The length was chosen to bridge the distance from the participant's hand to the end of the scanner bore. The design was inspired by the piano-key mechanism. When the operator presses one side down, the other side will rise up to stroke the participant's digits. (Photo credit: Yinghua Yu, Okayama University)

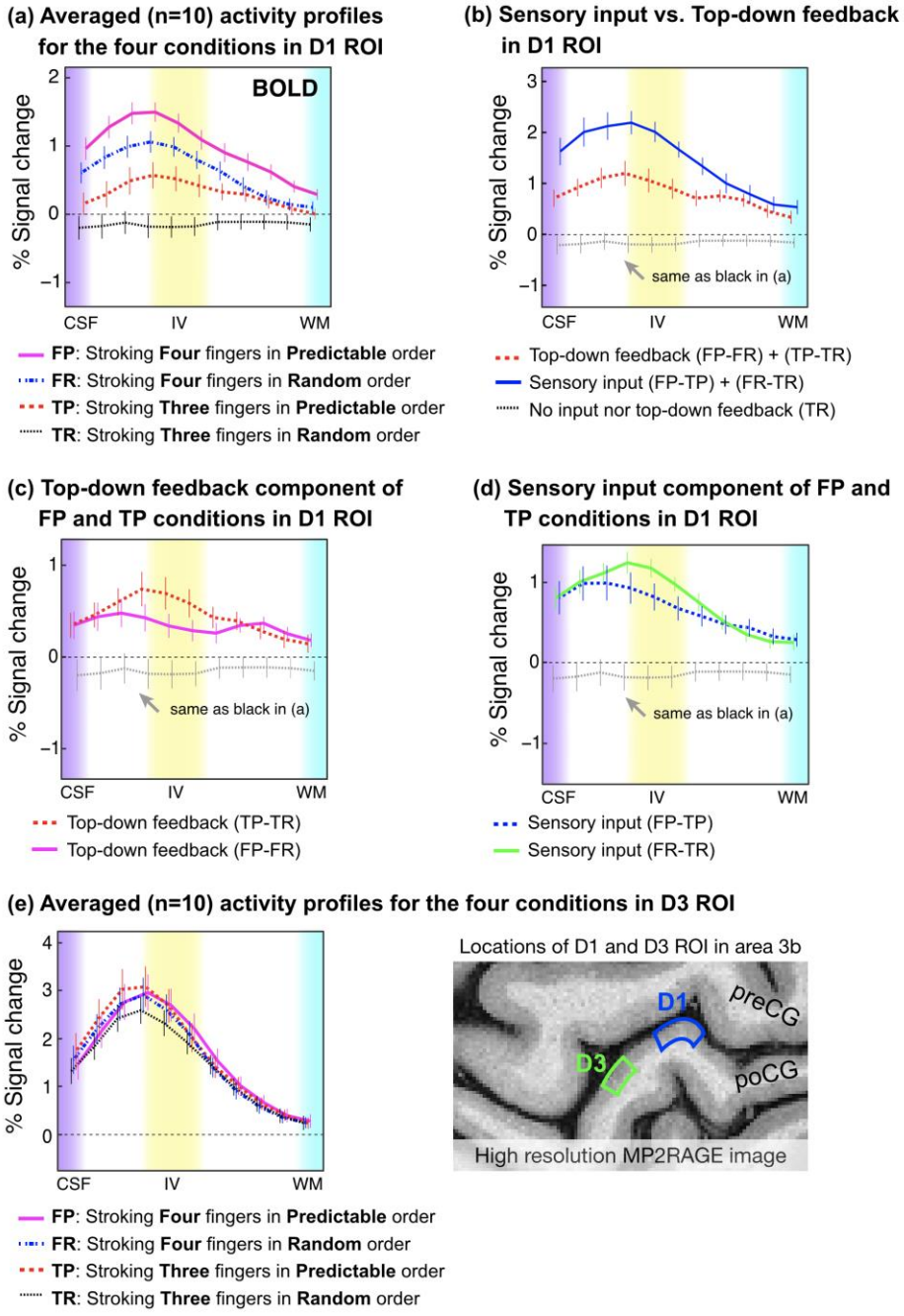

Fig. S3. Cortical profiles of BOLD activity changes in ROI of the index finger in area 3b. The BOLD results do not show clear qualitative layer-dependent differences compared to VASO (see Fig. 4). As such, the layer-dependent BOLD profiles for sensory input and top-down feedback in panel (b) look very similar in BOLD. They both peak in upper layers and look like scaled versions of each other. This is different for the corresponding VASO profiles in Fig. 4(b). The VASO profiles peak at different cortical depth and are statistically independent (Table S1.). The fact that VASO can better discriminate task condition from layer profiles than BOLD, has been previously shown and quantified in our previous study (*15*). These data are shown for the sake of completeness only. The main results that are used to draw the conclusions of the layer-dependent activity are given in Fig. 4.

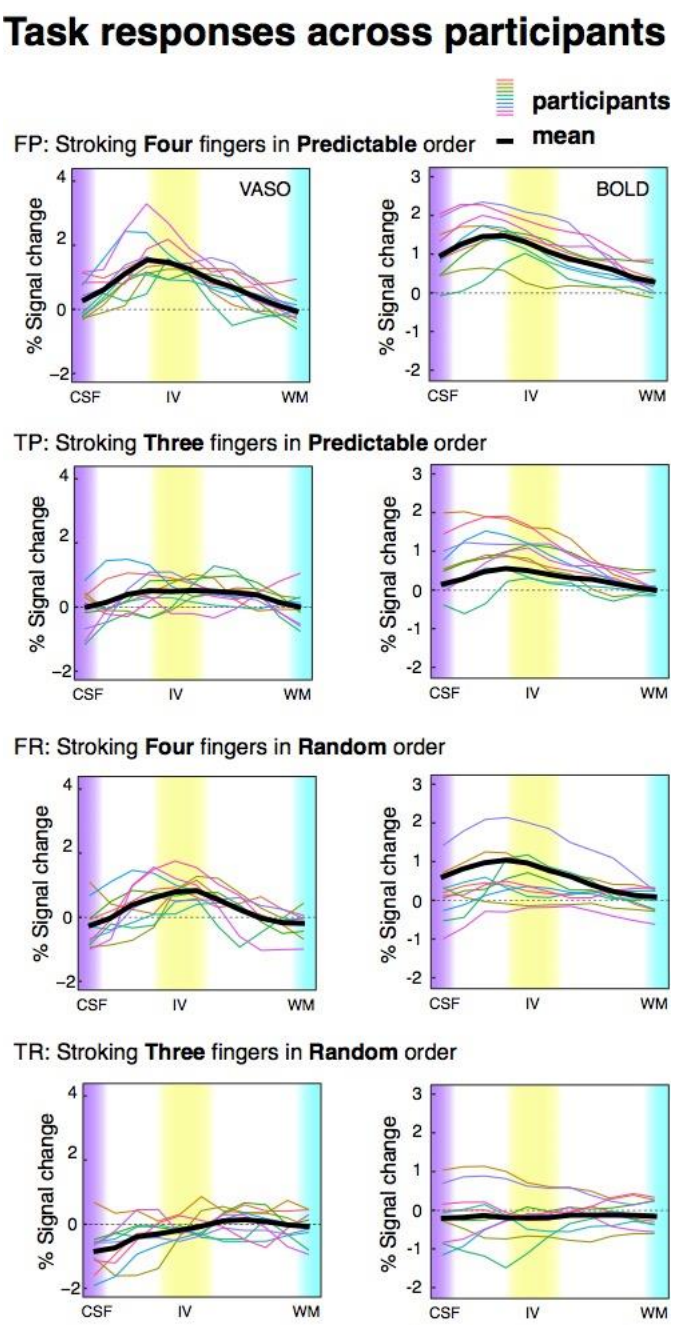

Fig. S4. Stability and repeatability of prediction task results across participants. Related to Fig. 4 for VASO and to fig. S3 for BOLD. The black lines represent the average across participants (n=10) which were the same as Fig. 4. The corresponding layer-profiles for different conditions of all participants for VASO and BOLD were plotted in each graph. Despite residual inter-participant variability, the cortical profiles are consistently modulated for the different task conditions. The high stability of the results across participants allows reliable interpretations of feed-forward and feedback circuitry. Comparing the two functional fMRI contrasts across the two columns reveals that BOLD is more dominated by superficial layers compared to VASO. This is expected due to the venous signal leakage of BOLD compared to VASO.

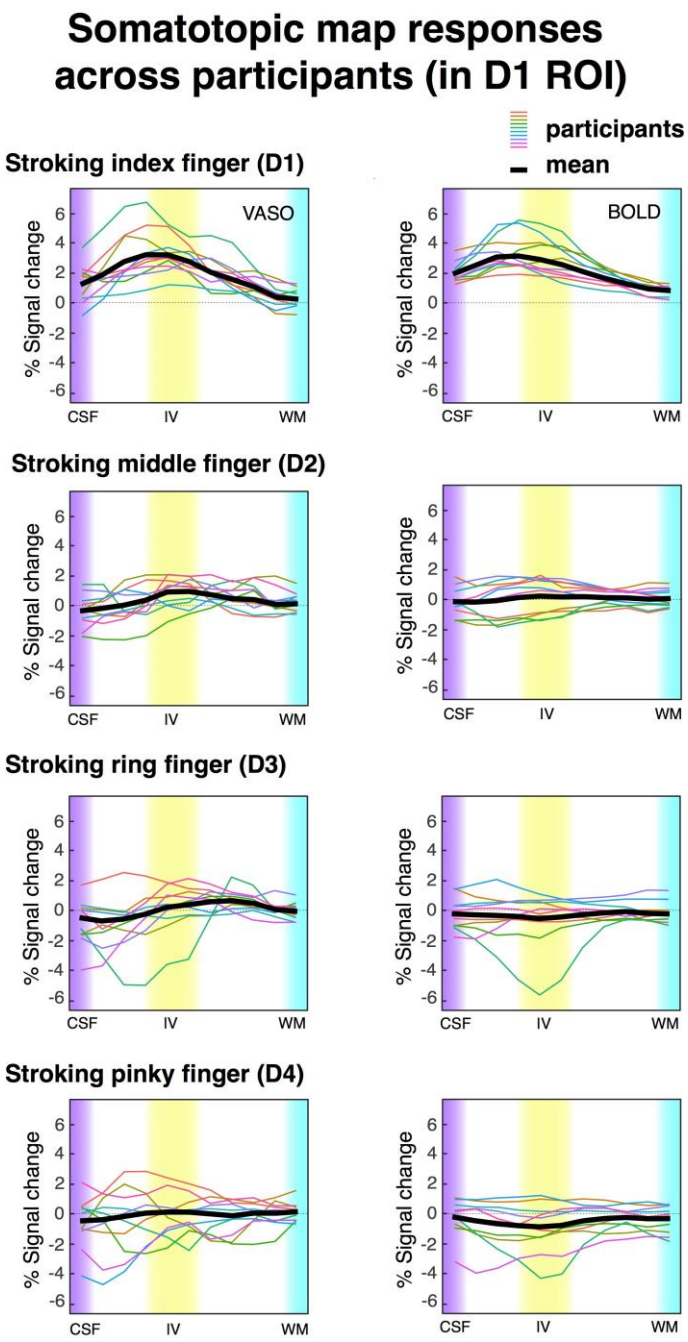

Fig. S5. Stability and repeatability of functional localizer across participants. Related to Fig. 2. The black lines represented the average across participants, which is the same as in Fig. 2. The corresponding layer-profiles for the different conditions of all participants for VASO and BOLD are plotted in each graph. Despite considerable inter-individual variability, the signal in the ROI of the index finger is increasing only for the stroking of the index finger. This confirms that the ROI-definition setup with the functional localizer can appropriately isolate the activity changes that refer to the index finger. With such high finger-specificity, we can focus our neuroscientific interpretations on sensory and prediction input of one finger without the need to account for cross-finger effects.

Table S1. Summary statistics of difference between task condition pairs of the VASO signal in each layer.
The difference between any pair of task conditions across the all layers were statistically assessed through a linear mixed-effects (LME) modeling approach using the R package nlme. With the pair-wise difference at each layer from each experiment session (N=10, two from the same participants) as the data for the response variable, the LME model was formulated with no intercept, with layers as a fixed-effects factor and with a random intercept for cross-participants variability. The F-statistic was used to test the null hypothesis of all involved layers having an effect size of zero. Here we only reported the t and p values for pair-wise comparison. The coloring in this table is match the layer coloring in Fig. 4.

Comparisons	**CSF**	**Superficial layers (L2/3)**			**Middle layer (L4)**		**Deeper layers (L5/6)**				**WM**
FP vs. FR	-	t=4.07 p<0.001	t=4.38 p<0.001	t=5.63 p<0.001	t=6.73 p<0.001	t=4.12 p=0.001	t=2.93 p=0.003	t=3.54 p=0.001	t=3.33 p=0.001	t=2.46 p=0.01	-
TP vs. TR	-	t=2.66 p=0.008	t=2.45 p=0.012	t=2.61 p=0.009	t=3.94 p=0.002	t=3.51 p=0.003	t=2.49 p=0.01	t=2.03 p=0.026	t=1.87 p=0.036	t=1.03 p=0.156	-
FP vs. TP	-	t=2.79 p=0.006	t=3.96 p<0.001	t=5.59 p<0.001	t=4.68 p=0.001	t=3.39 p=0.004	t=2.12 p=0.022	t=1.17 p=0.127	t=0.08 p=0.468	t=0.05 p=0.48	-
FR vs. TR	-	t=2.48 p=0.012	t=2.94 p=0.004	t=3.55 p=0.001	t=8.19 p<0.001	t=7.49 p<0.001	t=2.65 p=0.007	t=0.58 p=0.283	t=-0.69 p=0.248	t=-0.87 p=0.197	-
(FP – FR) + (TP - TR) vs. (FP – TP) + (FR - TR)	-	t=-0.75 p=0.227	t=0.17 p=0.432	t=0.73 p=0.235	t=1.79 p=0.039	t=1.71 p=0.046	t=0.16 p=0.435	t=-1.26 p=0.106	t=-2.24 p=0.014	t=-1.66 p=0.049	-