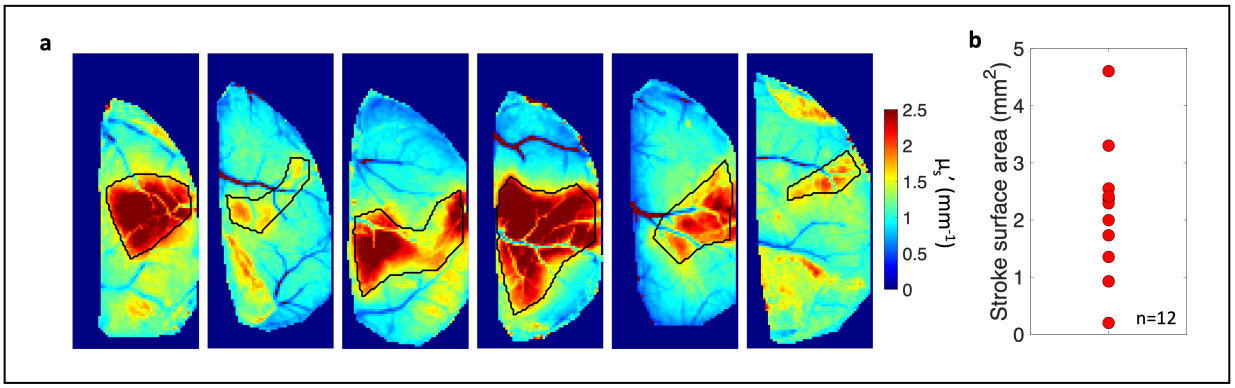
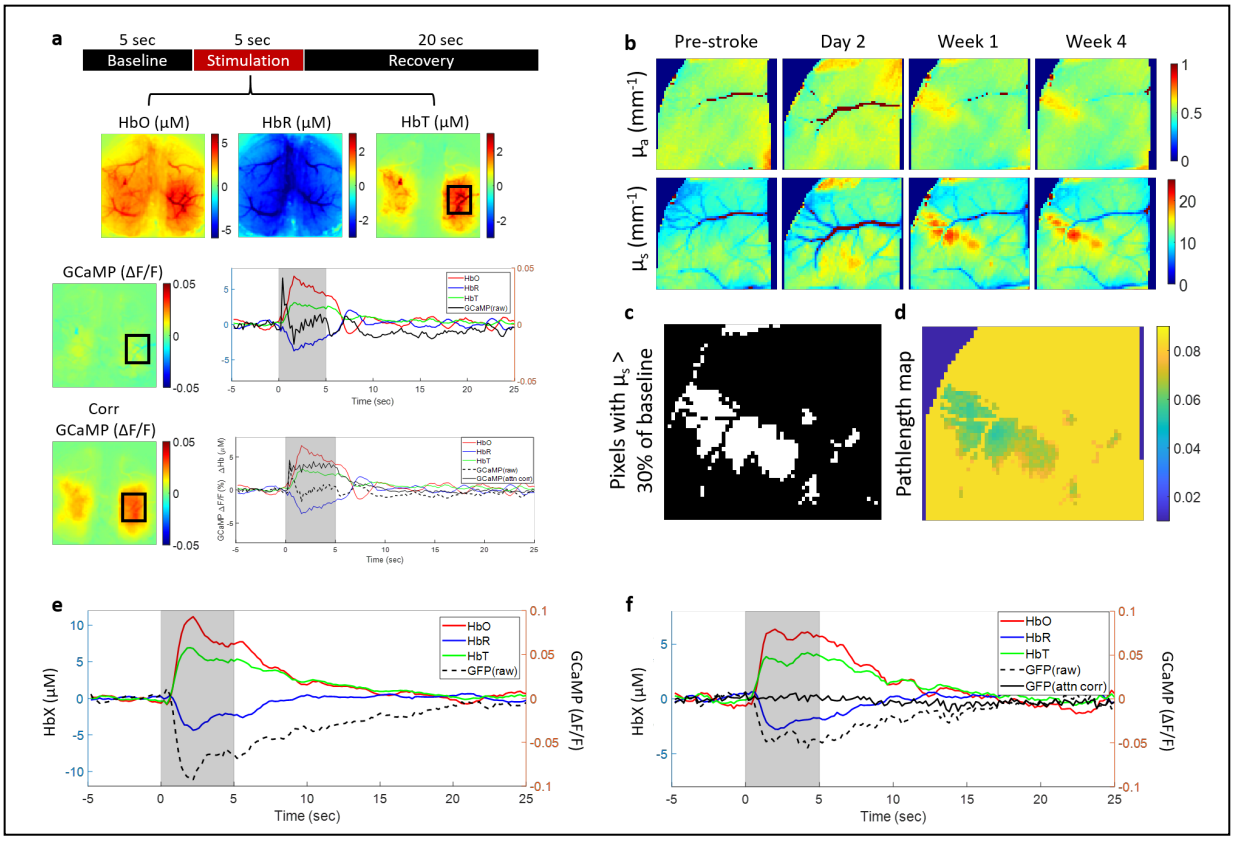
Supplementary Material

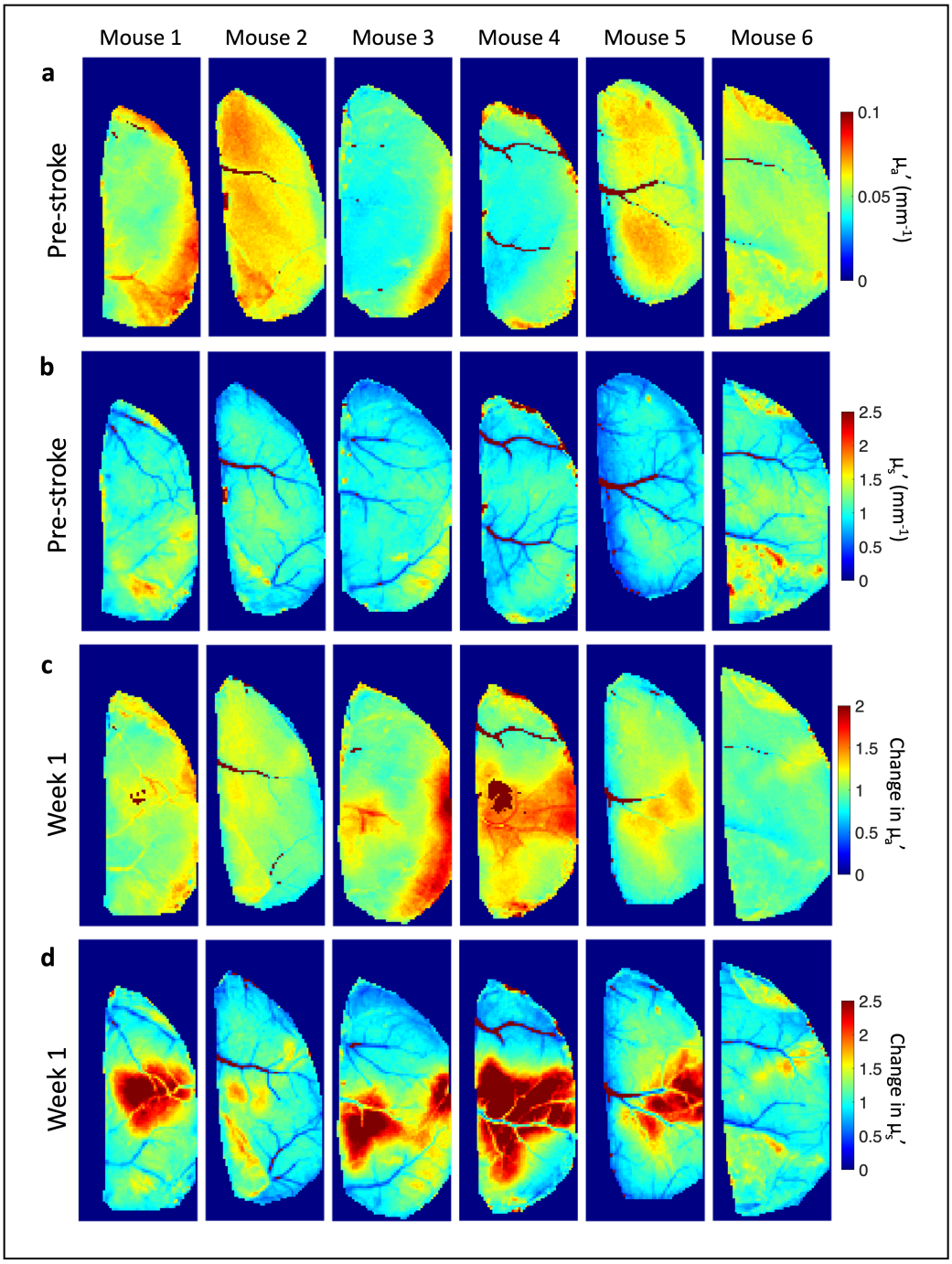


Supplementary figure 1: Targeted photothrombosis results in variable stroke area. (a) Scattering coefficient maps at Week1 with stroke core outline in black. (b) Surface area of the stroke core for all mice (n=12).

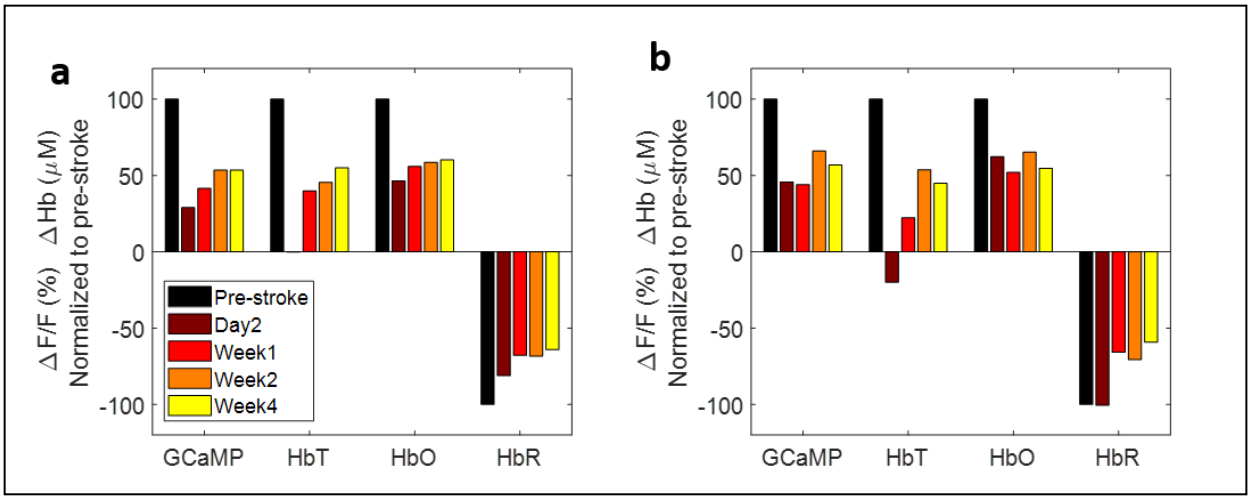


Supplementary figure 2: Fluorescence correction for hemodynamic crosstalk. (a) Top: Block design of single sensory stimulation trial and spatial hemodynamic response maps for HbO, HbR, and HbT. Middle: Raw GCaMP response map during 5 sec of sensory stimulation and time course of trial averaged data for GCaMP and hemodynamics from ROI marked in black box. Uncorrected GCaMP shows rise in fluorescence at the start of stimulation but begins to decrease with the rise of hemodynamic response. Bottom: Spatial map of GCaMP corrected for hemodynamic crosstalk. Note the appearance of response compared to uncorrected GCaMP in spatial map. Time course of corrected GCaMP overlaid with uncorrected GCaMP and hemodynamics. Note that GCaMP is now elevated for the full stimulation period. (b) Absorption and scattering coefficients obtained from SFDI before and after stroke and used in the correction algorithm in the form of pathlength factor. Stroke leads to increases in the scattering signal that needs to be accounted for accurate correction due to its effect on pathlength. (c) Binary maps of all pixels that have scattering coefficient greater than 30% of baseline scattering. The scattering and absorption coefficients from these pixels are used in the Monte Carlo simulation to obtain pathlength. (d) Spatial map of pathlength factors obtained from Monte Carlo simulations and used in the correction algorithm. (e,f) Validation of correction algorithm with cellular fluorescent marker GFP. (e) GFP signal

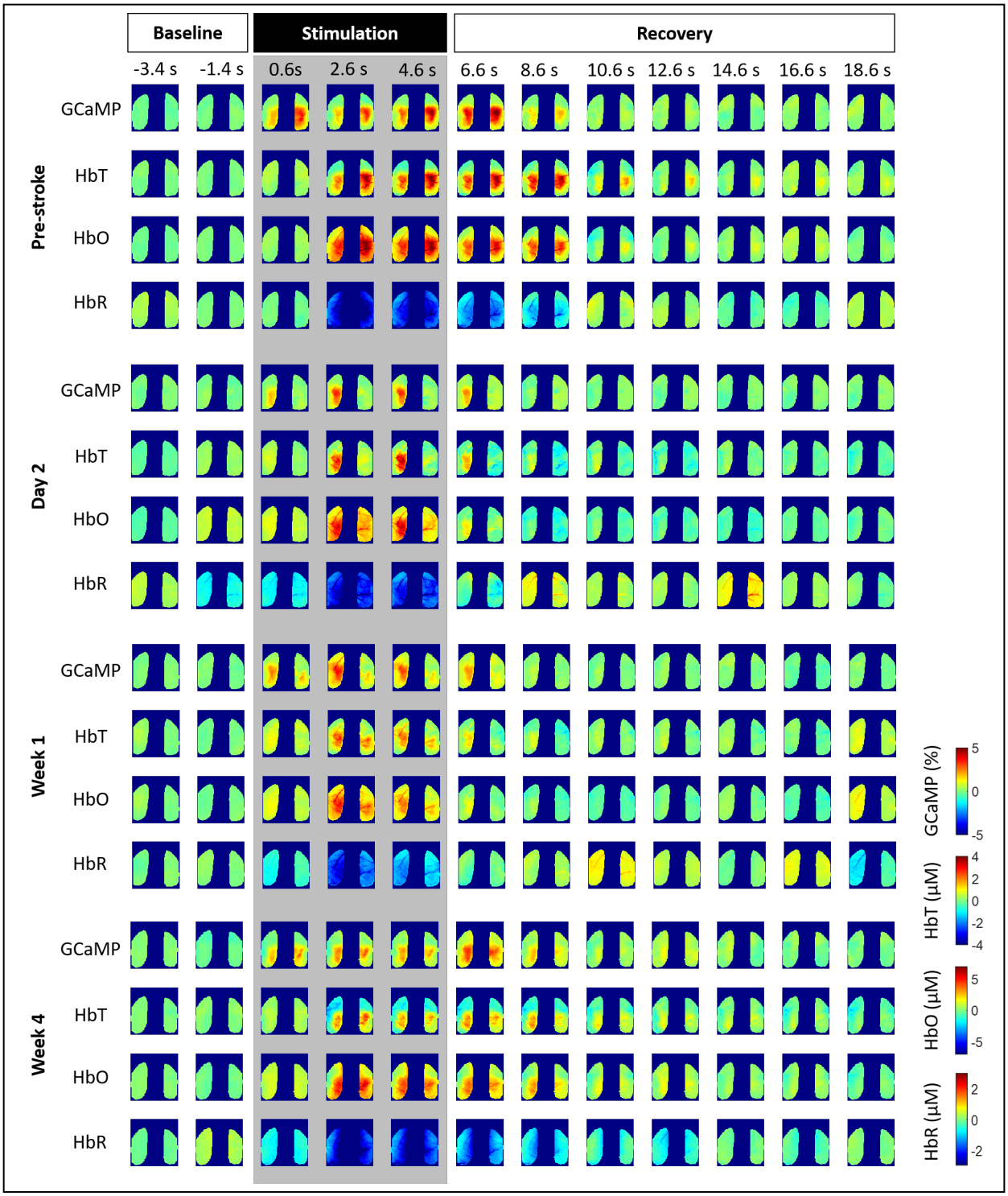
overlaid with hemodynamics during 5sec of sensory stimulation. GFP drops in association with hemodynamic increase. (f) Correction applied to GFP signal during sensory stimulation. Corrected GFP is a flat line as expected since GFP fluorescence is not altered with neural activity or hemodynamics.



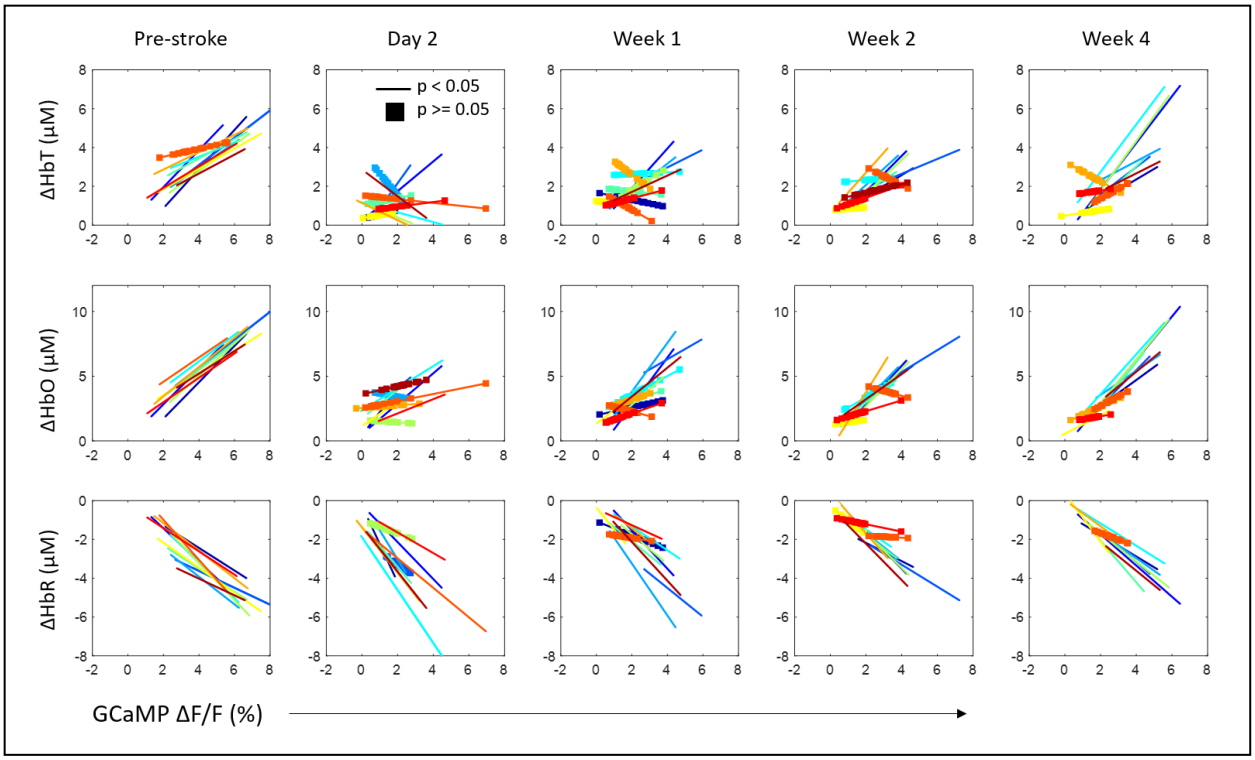
Supplementary figure 3: SFDI maps of optical properties in the ipsilateral hemisphere for 6 mice. (a) Absorption coefficient pre-stroke. (b) Scattering coefficient pre-stroke. (c) Change in absorption coefficient at week1 from pre-stroke. (d) Change in scattering coefficient at week1 from pre-stroke.



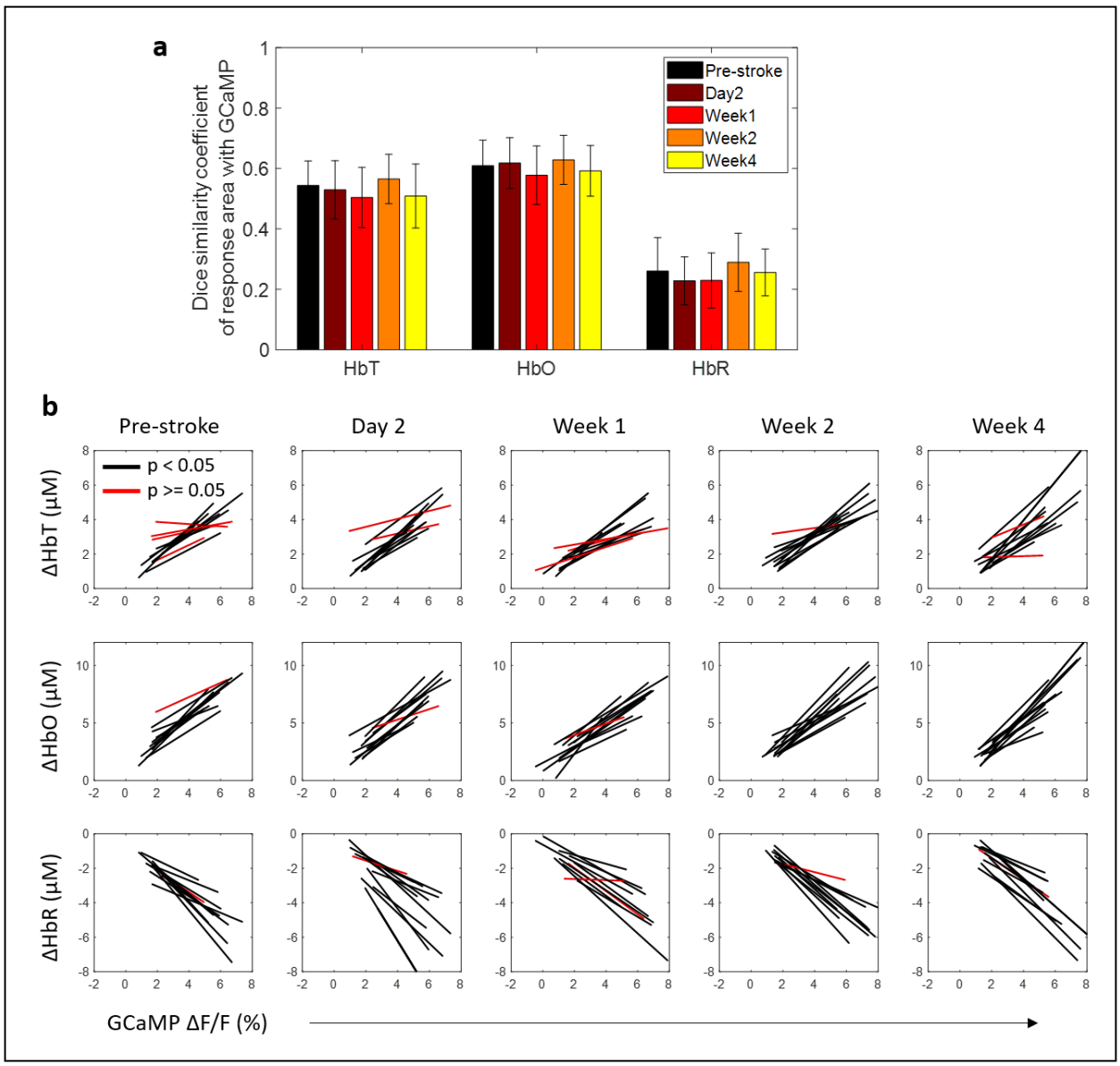
Supplementary figure 4: Responses in the affected hemisphere normalized to pre-stroke during stimulation of the impaired (a) and unimpaired (b) forelimb. HbT response is more sensitive to the stroke compared with HbO and HbR.



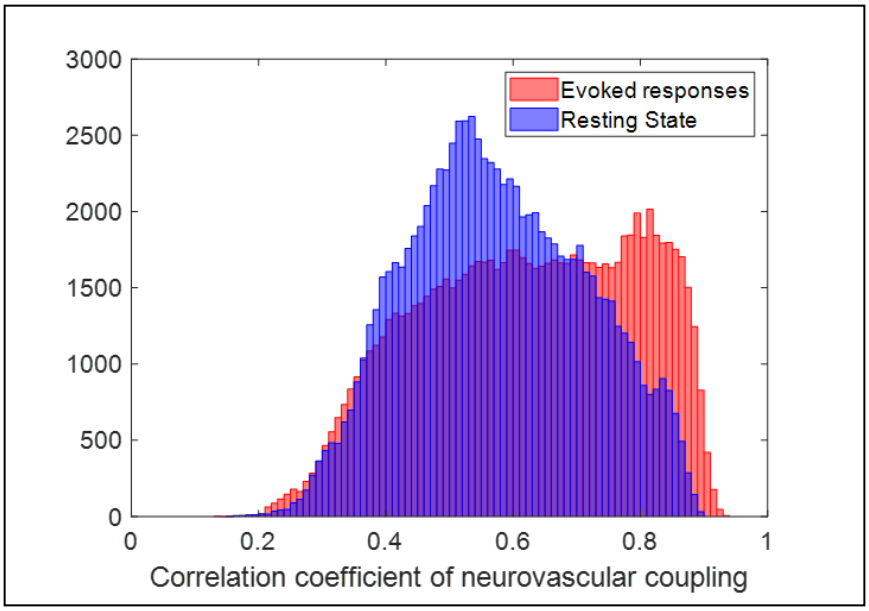
Supplementary figure 5: Spatial maps of GCaMP and hemodynamic responses over time during sensory stimulation. Lesion in the right hemisphere.



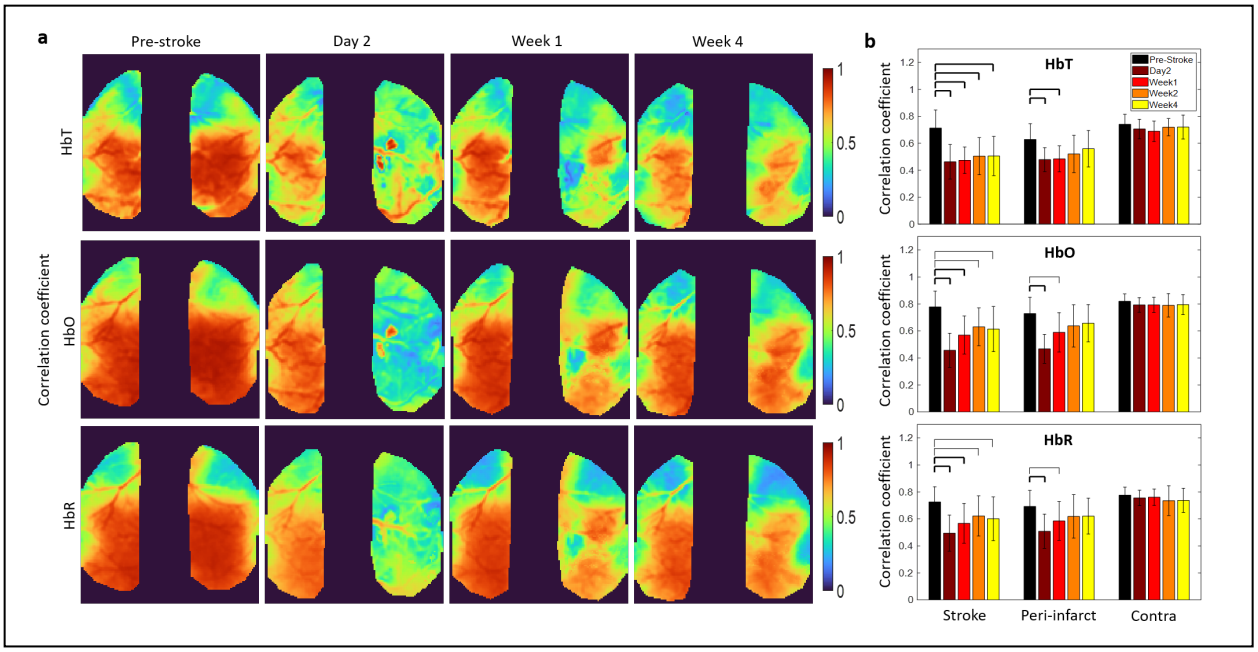
Supplementary figure 6: Correlation of calcium and hemodynamic evoked responses to sensory stimulation of the affected forelimb color-coded by mouse. Mice with significant correlation in response magnitudes of calcium and hemodynamics are shown as solid lines and mice whose responses were not correlated are shown with filled squares. Note that the animals that did not show correlation at week 4 after stroke also lacked correlation in the acute phase of stroke at week 1.



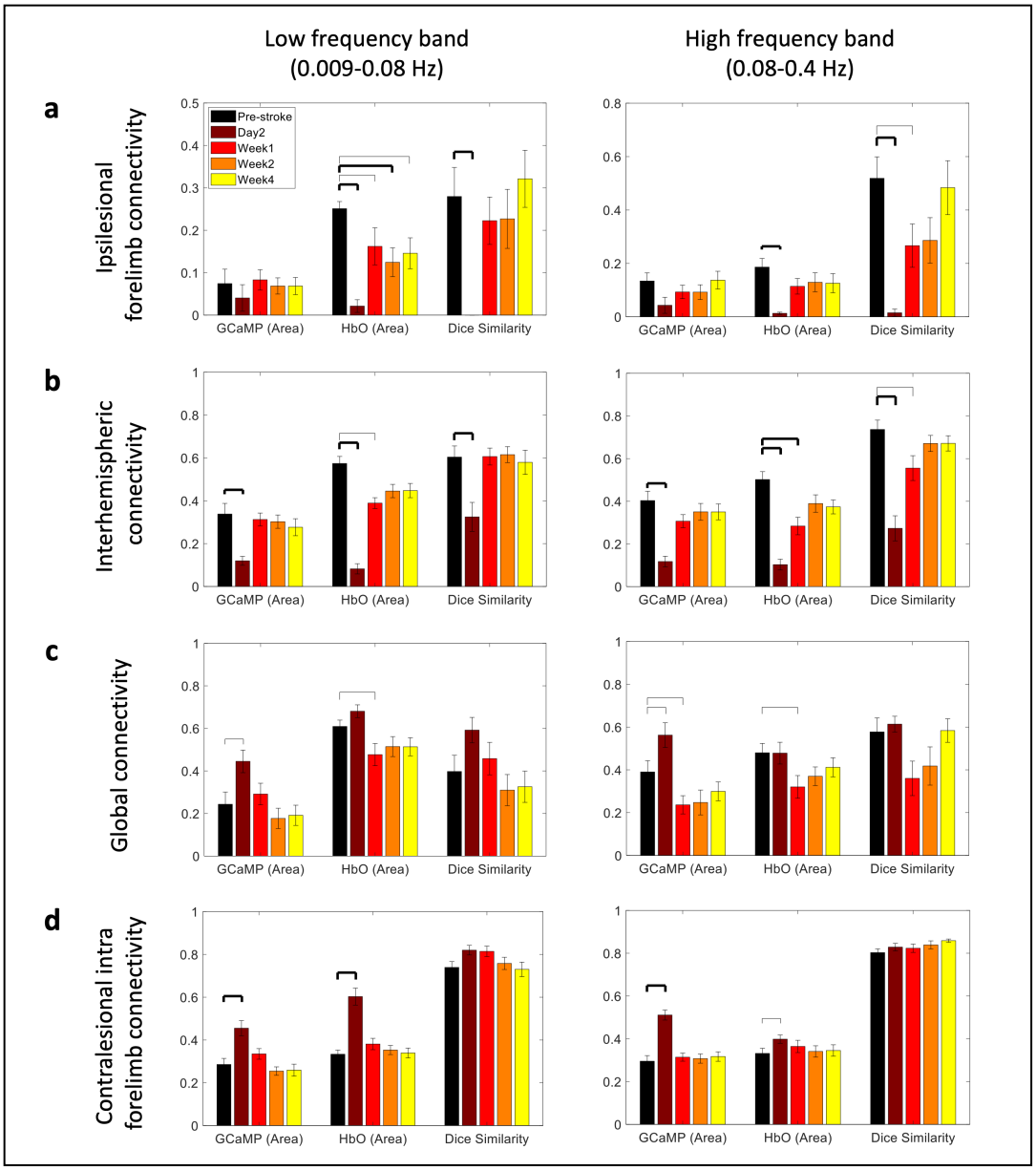
Supplementary figure 7: Responses within the unaffected hemisphere during stimulation of the unaffected forelimb. (a) Dice similarity coefficient between GCaMP response areas with each hemodynamic measure. There was no change in similarity of response area after stroke. (b) Correlation of calcium and hemodynamic evoked responses in the unaffected forelimb to sensory stimulation of the unaffected forelimb.



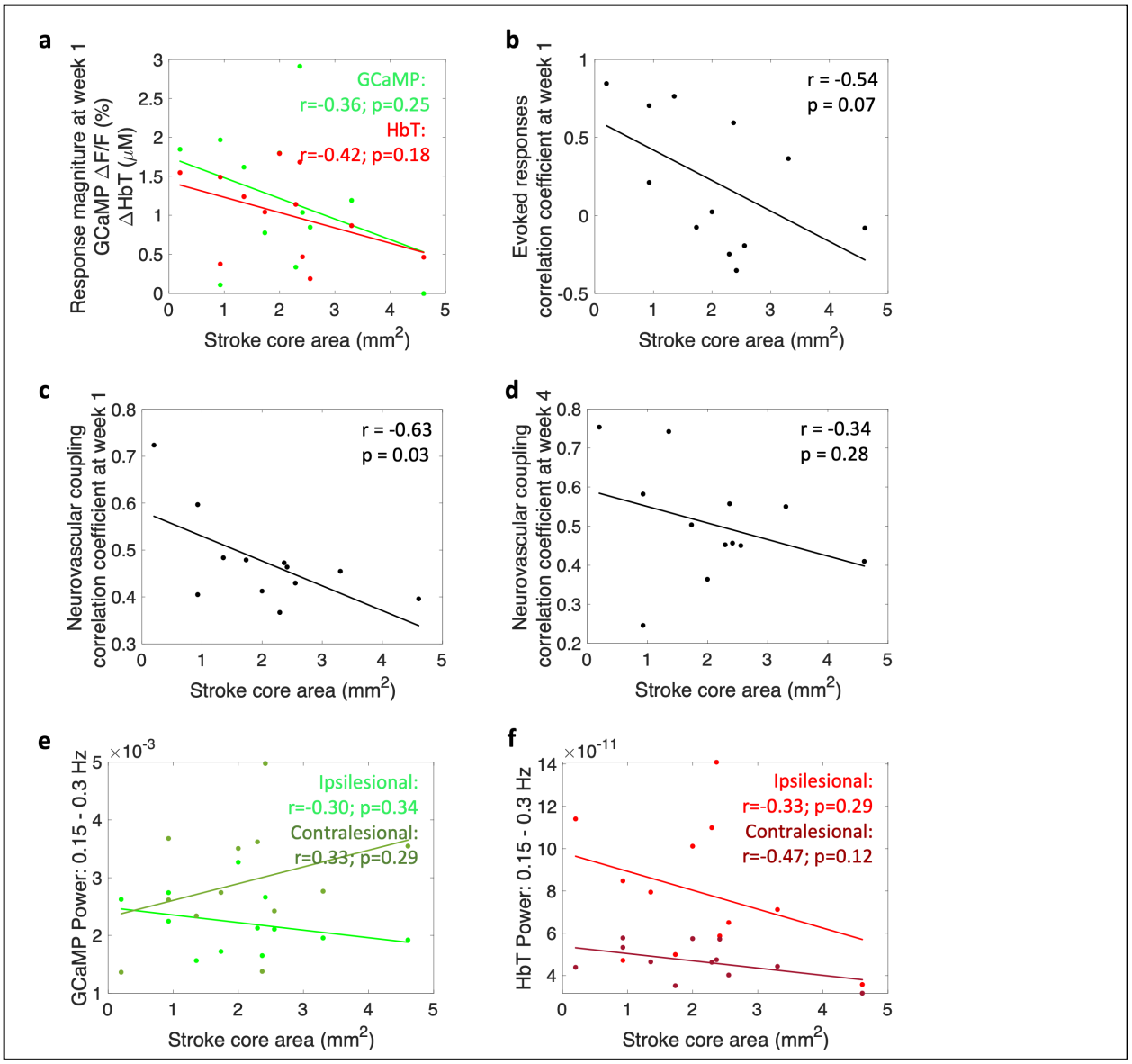
Supplementary figure 8: Pearson's correlation coefficient of neurovascular coupling in healthy pre-stroke animals during sessions with evoked responses and resting-state sessions.



Supplementary figure 9: (a) Pixel-by-pixel Pearson's correlation coefficient between measured and predicted HbT (top), HbO (middle), and HbR (bottom). Predicted HbX is obtained by convolving the GCaMP signal at each time point with the HRF obtained for that specific time point and pixel. (h) Pearson's correlation coefficient quantified across all mice within the stroke core, peri-infarct, and contralesional forelimb region. Thick bars: $p<0.01$, thin bars: $p<0.05$.



Supplementary figure 10: RSFC proportional area and dice coefficient analysis at threshold of 0.4. Each figure shows the proportional area of GCaMP and HbO above the correlation coefficient equal to 0.4 and the dice similarity between the GCaMP and HbO at 0.4. (a) Forelimb homotopic connectivity in the low frequency band (left) and high frequency band (right). (b) Interhemispheric connectivity in the low frequency band (left) and high frequency band (right). (c) Global connectivity in the low frequency band (left) and high frequency band (right). (d) Contralesional forelimb intrahemispheric connectivity in the low frequency band (left) and high frequency band (right).



Supplementary figure 11: Correlation between neuroimaging measures and the stroke core area at Week1. (a) Response magnitude of GCaMP and HbT. (b) Correlation coefficient of evoked responses. (c) Neurovascular coupling correlation coefficient at week1. (d) Neurovascular coupling correlation coefficient at week4. (e) Oscillation power of GCaMP in the ipsilesional and contralesional hemispheres. (f) Oscillation power of HbT in the ipsilesional and contralesional hemispheres.

		Pre-stroke	Day0	Day2	Week1	Week2	Week4
Mouse 1	Impaired	32	0	4	0	4	2
	Unimpaired	79	4	17	12	37	55
Mouse 2	Impaired	40	8	20	17	22	11
	Unimpaired	48	15	27	23	37	12
Mouse 3	Impaired	44	2	2	5	4	5
	Unimpaired	79	12	16	38	24	10
Mouse 4	Impaired	55	3	12	48	15	28
	Unimpaired	49	12	11	30	16	31
Mouse 5	Impaired	49	3	34	15	34	43
	Unimpaired	28	15	19	63	31	45
Mouse 6	Impaired	31	8	8	3	5	3
	Unimpaired	77	33	49	15	19	15
Mouse 7	Impaired	38	1	13	7	9	10
	Unimpaired	30	3	23	31	14	14
Mouse 8	Impaired	66	0	6	2	5	3
	Unimpaired	54	1	9	21	70	106
Mouse 9	Impaired	51	3	24	11	5	10
	Unimpaired	69	7	28	25	27	17
Mouse 10	Impaired	28	10	6	26	12	19
	Unimpaired	13	6	7	21	21	10
Mouse 11	Impaired	36	1	5	1	9	13
	Unimpaired	84	9	28	22	19	42
Mouse 12	Impaired	62	1	26	26	39	18
	Unimpaired	34	2	16	18	10	16

Supplementary table 1: Raw limb use rears in the cylinder test at each time point before and after stroke.