Utilizing multimodal MRI to detect somatosensory stimulation in the rabbit

Magnetic resonance imaging (MRI) is a powerful tool to investigate neural processing. Utilizing animal models enables research that is difficult to perform in humans. However, some animal models require anesthesia or sedation when undergoing MRI which negatively impacts the cognitive state of the animal and the physiology underlying hemodynamic correlates of neural activity.

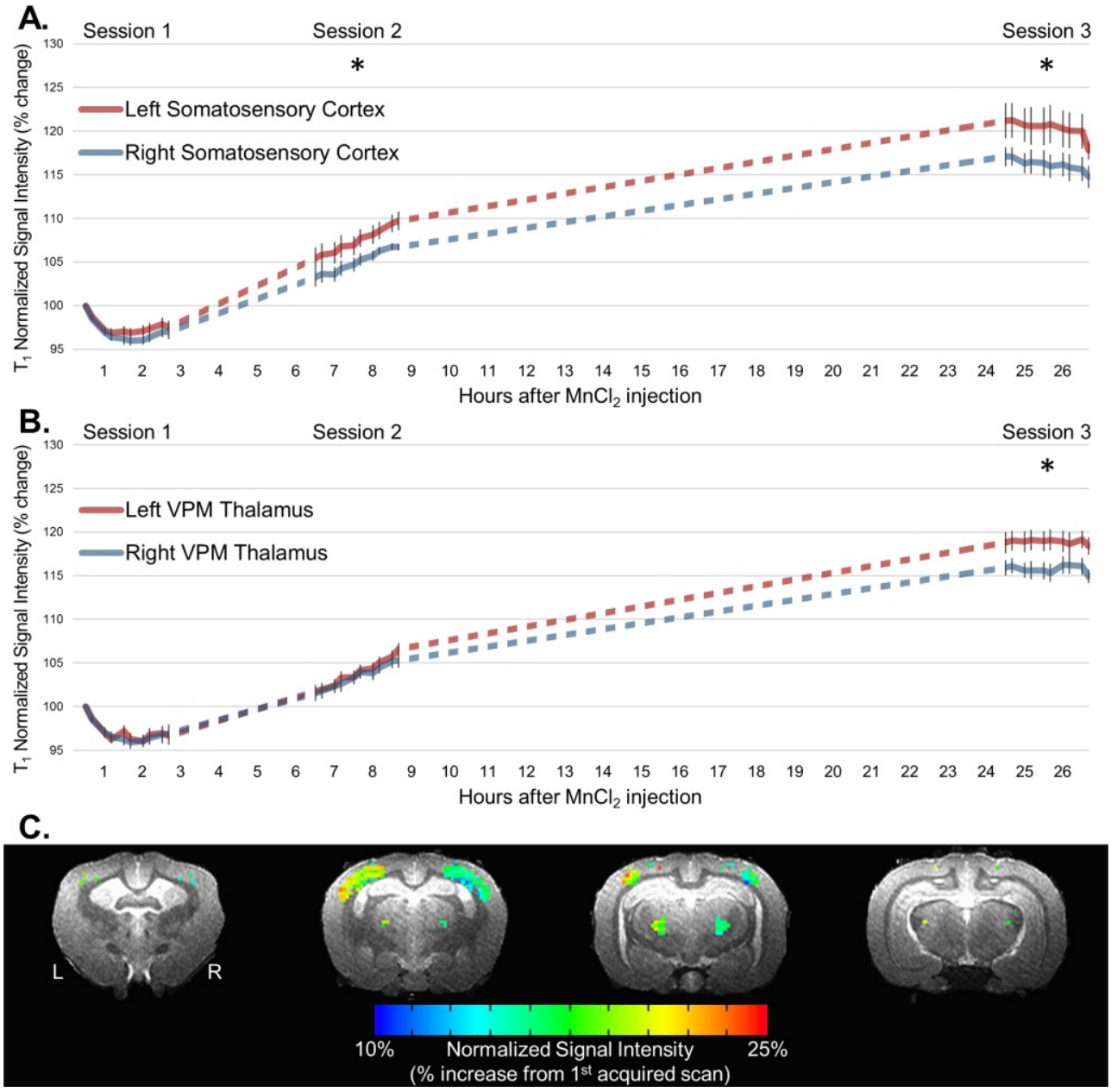

Fig. 1. BOLD activation in response to right whisker vibration. A. Mask of significantly active voxels in the contralateral whisker-related somatosensory cortex and ventral posteromedial thalamus during vibration of right whiskers in rabbits (n=10). B. Spatial map of visual cortex control regions of interest. C. BOLD percent signal change (mean ± SEM) in the somatosensory cortex, ventral posteromedial nucleus of the thalamus, and visual cortex. The contralateral somatosensory system has significantly greater BOLD response compared to the ipsilateral side. The visual cortex shows minimal, non-significant BOLD response during whisker stimulation. Asterisks denote significant difference between hemispheres. D. Representative time course profiles (mean ± SEM) of the three regions during whisker vibration.

Activity-induced manganese-dependent MRI (AIM-MRI) is a powerful tool to track system-wide neural activity using high resolution, quantitative T1-weighted MRI in animal models. Because manganese (Mn^{2+}) acts as a calcium analogue, AIM-MRI is more directly attributable to neuronal activation than the blood-oxygen-level dependent (BOLD) response. With AIM-MRI, Mn^{2+} ions enter neurons via preferentially active voltage-gated calcium channels. The more active a neuron is, the more Mn^{2+} will accumulate and the more the MR signal intensity will change. Once inside a neuron, Mn^{2+} becomes temporarily sequestered by binding to proteins and nucleic acids. Studies utilizing AIM-MRI can either be performed inside or outside of the MRI environment using still or free-moving animals since Mn^{2+} accumulation can be assessed via MRI at a later time representing a “snapshot” of the regions that were activated by the experimental manipulation.

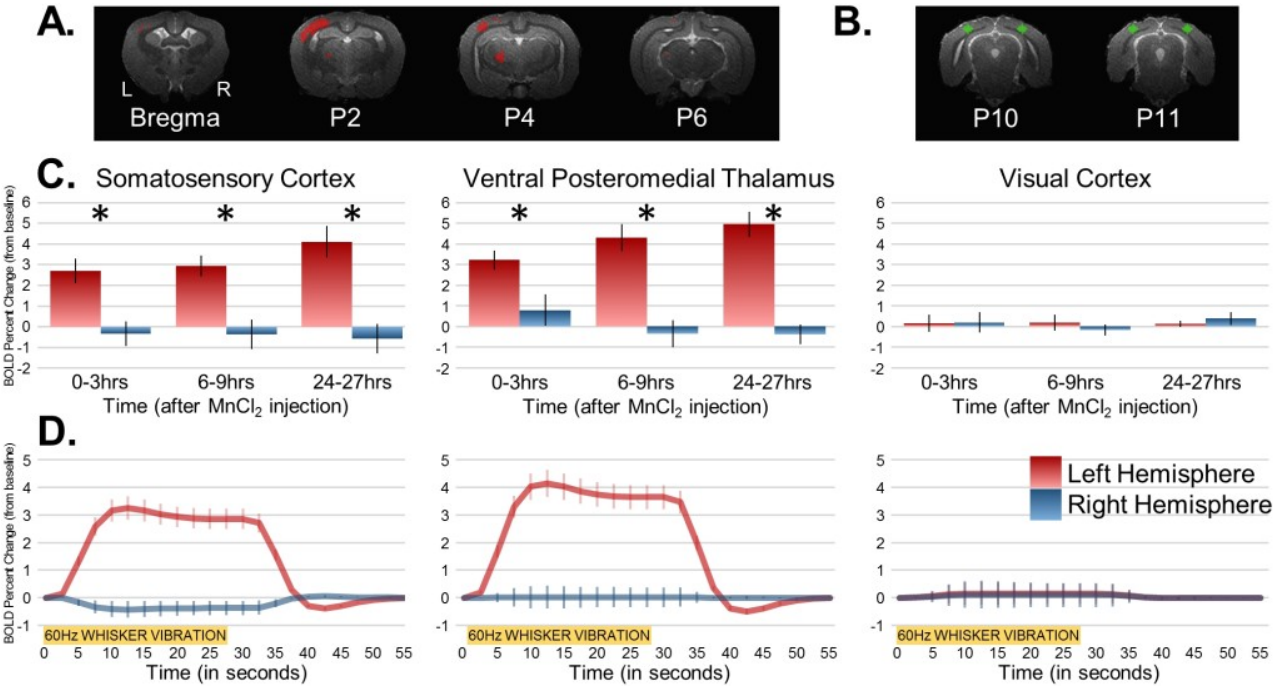

Fig. 2. T1W signal intensity profiles and color maps of somatosensory cortex and VPM thalamus

showing significant differential Mn2+ accumulation. A. T1W signal intensity profile (normalized to pituitary gland and relative to first scan from first session) from somatosensory cortex (mean ± SEM). Asterisks denote significant post-hoc hemispheric differences during 6-9 hrs (2nd) and 24-27 hrs (3rd) post-injection session (p less than .05). Red line = Left somatosensory cortex (contralateral to right whisker vibration), Blue line = Right somatosensory cortex (ipsilateral to right whisker vibration). Dotted lines denote time spent in home cage between sessions and is meant to provide a “guide to the eye”. B. T1W signal intensity profile (normalized to pituitary gland) from ventral posteromedial nucleus of the thalamus (mean ± SEM). Asterisk denotes significant post-hoc hemispheric differences during 24-27 hr (3rd) post-injection session (p less than .05). Red line = Left VPM thalamus (contralateral to right whisker vibration), Blue line = Right VPM thalamus (ipsilateral to right whisker vibration). Linear curve-fitting method employed. C. Color maps from the end of session 3 displaying significant accumulation on Mn2+ in the left somatosensory cortex and VPM thalamus relative to right hemisphere.

Few studies have provided a systematic evaluation of the factors influencing the detection of Mn^{2+} such as dosage and the temporal characteristics of Mn^{2+} uptake. In our study, we identified an optimal dose of Mn^{2+} that minimized the toxic effects of Mn^{2+} but enabled the detection of Mn^{2+} accumulation in active neural regions of the rabbit. T1-weighted MRI and functional MRI were collected 0-3, 6-9, and 24-27h post-Mn^{2+} injection while the whiskers on the right side were vibrated. Significant BOLD activation in the left somatosensory (SS) cortex and left ventral posteromedial (VPM) thalamic nucleus was detected during whisker vibration. T1-weighted signal intensities were extracted from these regions, their corresponding contralateral regions and the visual cortex (to serve as controls). A significant elevation in T1-weighted signal intensity in the left SS cortex (relative to right) was evident 6-9 and 24-27h post-Mn^{2+} injection while the left VPM thalamus showed a significant enhancement (relative to the right) only during the 24-27h session. Visual cortex showed no hemispheric difference at any timepoint. Our results suggest that studies employing AIM-MRI would benefit by conducting experimental manipulations 6-24h after subcutaneous MnCl2 injections to optimize the concentration of contrast agent in the regions active during the exposure.

Publication

Activity-induced manganese-dependent MRI (AIM-MRI) and functional MRI in awake rabbits during somatosensory stimulation.
Schroeder MP, Weiss C, Procissi D, Wang L, Disterhoft JF.
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