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ICMRI 2026
THE 14th INTERNATIONAL CONGRESS ON MRI
& 37th ANNUAL SCIENTIFIC MEETING OF KSMRM

AUGUST 27 - 28, 2026
Grand Walkerhill Seoul, Seoul, Korea
https://icmri.ksmrm.org/2026m

KSVMI-KSMRM

Joint03-2

Non-Human Primate fMRI for Whole-Brain Mapping and Causal Perturbation: From Anesthetized Microstimulation to Awake Behaving Imaging

전뇌 매핑과 인과적 조작을 위한 비인간 영장류 fMRI: 마취 하 미세전기자극에서 각성·행동 중 영상화까지

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Functional MRI in non-human primates enables direct cross-species comparison and, when combined with focal perturbation, supports causal inference about a region's functional role beyond correlational analysis. Here we establish a macaque fMRI platform spanning two complementary regimes: electrical microstimulation (EM)–fMRI for thalamocortical mapping in anesthetized animals, and awake behaving fMRI linking whole-brain activity to behavior.

In the first experiment, we stimulated the motor thalamus with a depth-advanceable microelectrode while recording whole-brain activity using MION-enhanced 7-tesla fMRI in three anesthetized rhesus macaques. Validating the approach, stimulation of the caudal ventral posterolateral nucleus (VPLc; 300 μA, biphasic 13-pulse trains at 130 Hz) strongly activated primary somatosensory cortex (28% of the S1 ROI), confirming the canonical VPLc–S1 projection. We then targeted the ventral lateral nucleus (VL) by advancing the electrode ventromedially during scanning. Given the reported somatotopy of VL and M1, we predicted that dorsolateral versus ventromedial VL stimulation would preferentially drive medial versus lateral M1. Consistent with the prediction, the dominant M1 activation centroid shifted laterally as the stimulation site advanced ventromedially (n = 2), indicating somatotopically organized motor thalamus–M1 connectivity aligned with the cortical homunculus. EM additionally co-activated pontine nuclei, cerebellum, and red nucleus; activation respected dentato-rubral anatomy, with contralateral dentate and ipsilateral red nucleus activity covarying. Higher-order nuclei (pulvinar, lateral posterior) evoked broad dorsal-stream and posterior parietal activation.

In the second project, we established awake behaving monkey fMRI using two canonical paradigms. We first trained a monkey to fixate centrally while viewing face stimuli; consistent with known face patches, we observed localized activation in the superior temporal sulcus, validating our setup and protocols. We then trained the memory-guided saccade task, in which the animal saccades to a remembered target location after a delay—a standard probe of working memory and oculomotor planning. Monitoring eye movements inside the scanner, the animal performed reliably, and we observed the predicted task-related activation in frontoparietal cortex.

Together, these results demonstrate an integrated non-human primate fMRI platform combining whole-brain imaging with causal microstimulation across anesthetized and awake behaving states, with implications for circuit-level systems neuroscience and precision deep brain stimulation.

Keywords: *Nonhuman primate, Functional MRI, Electrical microstimulation, Thalamocortical pathway, Effective connectivity*