BIMODAL FMRI FOR EXPLORING BRAIN ACTIVITY: A STRIATAL CBV RESPONSE ACCOMPANIED BY ENHANCED NIGROSTRIATAL ACTIVITY DETECTED BY MEMRI

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Introduction:

Functional MRI (fMRI) techniques are useful tools for assessing changes of the brain activity. Among them, hemodynamics based fMRI reveals vascular changes coupled to neural activation whereas manganese-enhanced MRI (MEMRI) detects neuronal activation with intracellular Ca^{2+} influx by using Mn^{2+} as a Ca^{2+} surrogate. Although the two methods are both commonly used to detect brain activation, the agreement of evidence derived from the two approaches has not been explored. Noxious electrical stimulation is known to induce negative CBV (cerebral blood volume) signals in the striatum (Shih, et al., 2009). The present study used this paradigm to investigate the convergence of CBV-weighted fMRI results with MEMRI findings, and proposed a bimodal fMRI protocol that may be used complementarily for exploring brain activity changes.

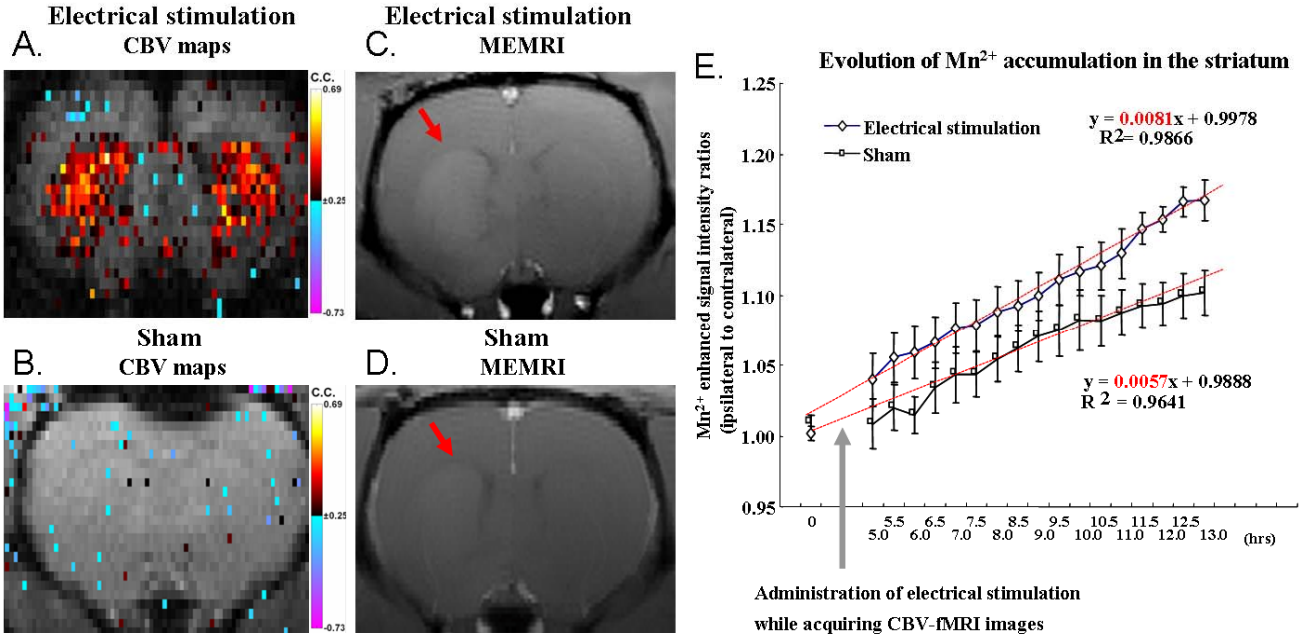
Materials and Methods:

CBV-weighted fMRI and MEMRI were carried out intrasubject. On the experiment day, 0.15 ul of 100 mM Mn^{2+} was microinjected into the left substantia nigra (SN) under 3% isofluorane anesthesia, followed by continuous intravenous infusion of alpha-chloralose (70 mg/kg) for the remaining time to maintain the anesthesia. Since the transport of Mn^{2+} takes hours, CBV-weighted fMRI was first performed after an intravenous injection of superparamagnetic iron oxide (SPIO) nanoparticles (*Resovist*, Schering, Berlin, Germany) as a contrast agent at a dose of 30 mg Fe/kg. A FLASH sequence was used with a repetition time of 150 ms, echo time of 20 ms, flip angle of 22.5°, field of view of 2.56 cm by 2.56 cm, slice thickness of 1.5 mm, 1 excitation, acquisition matrix of 128 by 64 (zero-filled to 128 by 128), and temporal resolution of 9.6 s per image. A series of 60 images was acquired during each scan. The first-, middle-, and last-20 time points corresponded to the off, on, and off statuses of the electrical stimulation, respectively. Resovist is known to have a blood half-life of 2.4–3.6 h. After the time, a FLASH sequence was used for MEMRI with a repetition time of 150 ms, echo time of 4 ms, flip angle of 60, field of view of 2.56 cm by 2.56 cm, slice thickness of 1.5 mm, 46 excitation, and acquisition matrix of 256 by 256. The total time for each scan was 30 minutes. MEMRI was performed for 12 hours.

Results and conclusions:

CBV responses were observed in the bilateral striatum after nociceptive electrical stimulation (Figure A). The sham group did not exhibit obvious CBV signals (Figure B). The group that received electrical stimulation showed more rapid Mn^{2+} transport along the nigrostriatal pathway as well as more Mn^{2+} accumulation in the striatum ipsilateral to the injection side of the SN, suggesting the noxious stimulus increased the activity of the nigrostriatal projection to the ipsilateral striatum. By contrast, the right striatum did not exhibit obvious Mn^{2+} accumulation. Figure C and D show the MEMRI images for the electrical stimulation and sham groups, respectively. Figure E shows the quantification of Mn^{2+} enhanced signals of the two groups.

MEMRI allows the detection of the activity of the traced pathway whereas fMRI responses mainly reflect changes in the local region. Therefore, the two methods can be used complementarily to detect the activity changes of a connect circuit. In the present study, we demonstrated that the striatal CBV responses captured by CBV-weighted fMRI were accompanied by enhanced nigrostriatal activity detected by MEMRI. The results not only support the agreement between the hemodynamics based fMRI and MEMRI, but also proposed a bimodal fMRI protocol that can be used complimentarily to explore brain activity.



References: Shih, Y.Y., Chen, C.C.et al., 2009. J Neurosci. 29,3036-44.