Detection of Spontaneous Pain due to Chronic Pain in the Rat

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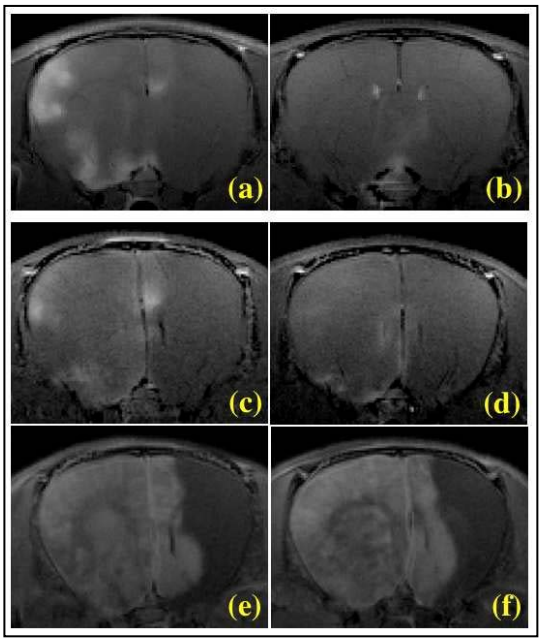
【Introduction】 Neuropathic pain is a complex, chronic pain state that usually is accompanied by tissue injury. Spontaneous pain and allodynia are the common complaint in chronic pain conditions. Spontaneous pain is either continuous or paroxysmal, and allodynia is pain triggered by innocuous stimuli. Non-invasive imaging techniques such as magnetic resonance imaging (MRI) are useful for the visualization of brain responses to pain. We have previously reported a study on the allodynia. However, the spontaneous pain is difficult for detection in the brain function using BOLD fMRI. It has been reported that activity-induced manganese-enhanced (AIM) MRI is not influenced by hemodynamic changes and can be used for brain functional observation. Manganese is good contrast agent for MRI. In AIM MRI, manganese enters neurons through voltage-gated Ca^{2+} channels during a neural activation and leads to signal enhancement in active brain areas. The purpose of this study is to detect brain activation spontaneous pain using AIM MRI in a segmental spinal nerve ligation (SNL) model.

【Materials and Methods】 The SNL model is an experimental model of chronic pain that accompanies the tactile allodynia. Male Sprague-Dawley (SD) rats (n = 10) were divided into two groups: SNL group (n = 5) and sham group (n = 5). The right L5 spinal nerves were isolated and ligated distal to the dorsal root ganglia and proximal to the sciatic nerve formation with 5–0 silk sutures. Sham-operated rats underwent a similar surgical procedure, except that spinal nerves were not ligated. Animals were examined using AIM MRI at two weeks after the surgery. Rats were anesthetized with 2.5 % isoflurane for surgery. Polyethylene catheter (PE-50) were placed in the femoral artery and the vein to monitor blood pressure, sample blood gases and administer drugs. The right external carotid artery was also cannulated for drug administration. The blood brain barrier was disrupted by rapidly injecting 20% D-mannitol through the carotid artery. This experiment does not provide a stimulus during infusing the 25 mM $MnCl_2$ solution. After the manganese administration, T_1-weighted images were acquired using a 4.7-T MRI system (Bruker) with the following parameters: spin-echo, repetition time (TR)/echo time (TE) = 400/10.5 ms, field of view (FOV) = 32 mm, and matrix size = 256 × 256, slice thickness = 1.0 mm, number of slices = 6, acquisition time for one set = 10 minutes. Image processing was performed using MRVision (MRVisoin Co., MA).

【Results and Discussion】



Spontaneous pain induced brain activation was successfully visualized using AIM MRI. Signal enhancement was observed in the contralateral side of the primary somatosensory area (S1) and ipsilateral side cingulate areas (Cg). S1 supports separation of various input. Cg is concerned with perception of pain. Therefore, these results suggest that the AIM MRI is useful for the depiction of the conducting pathway of pain. Furthermore, it may be useful for investigation of the neural connections that receive and modulate pain signals. Diagnostic imaging of chronic pain will play an important role in the clinical treatment of pain and the development of pain-relieving drugs.

The typical images of the activity-induced manganese-enhanced (AIM) MRI

(a) SNL model: brush stimulation of the right hind leg sole.
(b) Sham-operated model: brush stimulation of the right hind leg sole.
(c) SNL model: no stimulation.
(d) Sham-operated model: no stimulation.
(e) SNL model: Glutamic acid administration for BBB check.
(f) Sham-operated model: Glutamic acid administration for BBB check.