A pharmaco-fMRI study on pain networks induced by electrical stimulation after sumatriptan injection

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Purpose: Sumatriptan, a drug widely used to alleviate migraine headaches, has several somatosensory adverse effects such as tactile allodynia. This paper mainly focused on whether sumatriptan could simultaneously affect both sensory and affective circuitries.

Methods: We investigated the responses of 12 healthy volunteers to electrical stimuli after being infused with either sumatriptan or saline. Using a double-blind crossover study design, we used functional magnetic resonance imaging (fMRI) to measure brain activation in different sections during electrical stimulation. The visual analogue scale (VAS) and short-form McGill pain questionnaire (SF-MPQ) were used to rate stimulation-evoked sensations and affections after sumatriptan and saline injection.

Results: Sumatriptan predominantly activates regions in the medial pain system, as well as smaller regions of the lateral pain system. These regions include the secondary somatosensory cortex (SII), anterior insular cortex, orbitofrontal cortex, medial thalamus, cerebellar supravermis, dentate nucleus, and the majority of the anterior cingulate cortex (ACC) (Fig. 2a). By contrast, activation following saline administration was observed primarily in the lateral pain system, including the primary sensory cortex, lateral SII, posterior insular cortex, anterior ACC, lateral thalamus and other areas (Fig. 2b). Importantly, we found that VAS ratings and MPQ scores increased following sumatriptan infusion but not after saline administration (Fig. 1).

Discussion: Several brain regions like SII, insular cortex, thalamus, and cerebellum demonstrated the segregated activation pattern with sumatriptan and saline injections, respectively, which suggested that the distinct types of nociceptive neurons may exist in the above-mentioned regions, and this was more or less in accordance with previous studies [1-4]. Data from VAS ratings and SF-MPQ scores also support the notion from a different perspective.

Conclusion: To our knowledge, this is the first study to investigate the mechanisms underlying the nociceptive effects of sumatriptan following innocuous electrical stimulation in humans. Our fMRI, VAS and SF-MPQ findings suggest that sumatriptan plays a significant role in affective dimension of pain, as well as a minor role related to sensory discrimination.

References:

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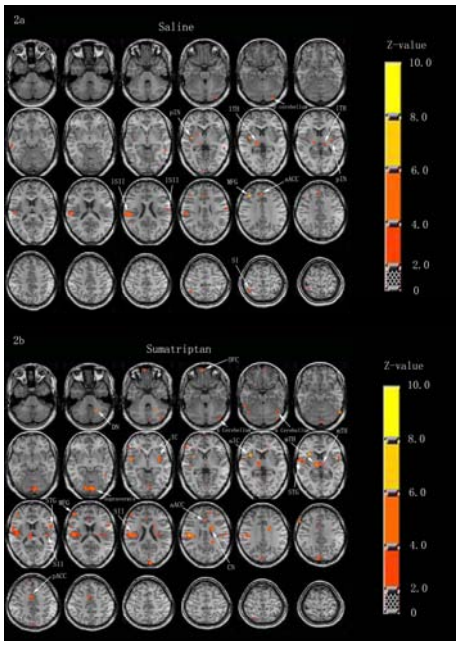

Fig.2 Several cortical and subcortical areas were engaged in the saline (**a**) and sumatriptan (**b**) conditions. More prominent activations were found in conditions sumatriptan than saline in the SII, anterior insular cortices (aIC), medial thalamus (mTH), ACC, and cerebellar supravermis. The color bar labels indicate levels of activation in the Z value (threshold at p = 0.01).

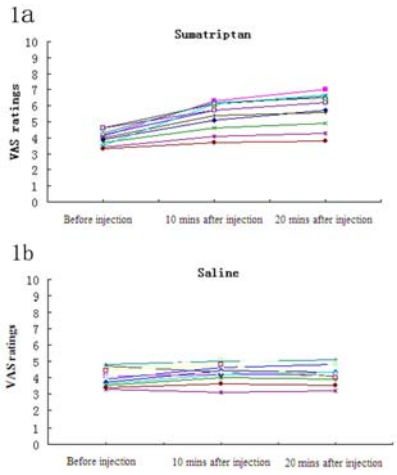

Fig.1 Median ratings with VAS in pre- and post-sumatriptan (**a**) and saline (**b**) conditions are shown for each subject. Significant differences were observed between data obtained before and after injection of sumatriptan ($p < 0.05$; Wilcoxon), not in saline condition.