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Voxel-based lesion symptom mapping (VLSM) in post-stroke complex regional pain syndrome

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Objectives

Complex regional pain syndrome (CRPS) of the hemiplegic upper limb is a painful and debilitating condition. CRPS after stroke is frequently encountered and interferes with the rehabilitation process and outcome. Post-stroke CRPS mostly occur from 1 to 5 months after stroke diagnosis, in which the period with the highest rehabilitation potential. Thus, early diagnosis and treatment of post-stroke CRPS is crucial. This study aims to investigate the neuroanatomical correlates associated with post-stroke CRPS using voxel-based lesion symptom mapping (VLSM) analysis.

Methods

We retrospectively screened patients from January 2013 to June 2019 who met the following criteria: first-ever ischemic stroke, unilateral and supra-tentorial lesion, and available brain magnetic resonance imaging (MRI) performed between 48 hours and 7 days after stroke. Total of 50 ischemic stroke patients' MRIs were selected for VLSM analysis and were divided into 2 groups; 27 patients were allocated to the CRPS group and 23 patients to the control group. The diagnosis of CRPS was based on revised International Association for the Study of Pain (IASP) diagnostic criteria and 3-phase bone scan confirmed the clinical diagnosis. For statistical purposes, we considered diagnosis of CRPS as a binary variable (absent/present) and generated statistic maps of lesion contribution. We investigated the neuroanatomical correlates of CRPS using VLSM analysis. Under the hypothesis that there are no significant differences between right- and left- hemispheric strokes, all lesion maps were flipped to one side in order to focus our analysis on lesion localization without regard to lateralization.

Results

In our patient group who were diagnosed as CRPS, 14 patients had lesions on the right cerebral hemisphere, and 13 patients on the left hemisphere, respectively. VLSM analysis revealed that presence of CRPS was significantly associated with the neuroanatomical structures including the insula, inferior parietal lobule (supramarginal gyrus and angular gyrus) and putamen. (Table 1) The statistical map was shown in Fig. 1.

Conclusion

Previous literatures reported the relationship between somatosensory dysfunction, proprioceptive impairment and post-stroke CRPS. Insula is known to have function in multimodal sensory processing and it is associated with persistent pain perception when impaired. Supramarginal gyrus is a structure that has a role in somatosensory function with proprioception and tactile sensory interpretation. And putamen is known to be involved in the processing of pain in humans. In this study, VLSM analysis suggested that insula, inferior parietal lobule and basal ganglia were associated with CRPS. These results suggested that lesion in brain structures related with sensory processing is important underlying pathomechanism of CRPS after stroke.

Table 1. The lesion map was co-registered and normalized using Statistical Parametric Mapping (SPM). Color-coded lesions on the brain were labeled according to anatomical region using the xjView 8 toolbox in SPM 12 software.

Dependent variable	Region	X	Y	Z	Voxels
Diagnosis of CRPS	Insula	-32	4	-10	22075
	Inferior parietal lobe	-34	-48	54	146
	Putamen	-26	12	10	26

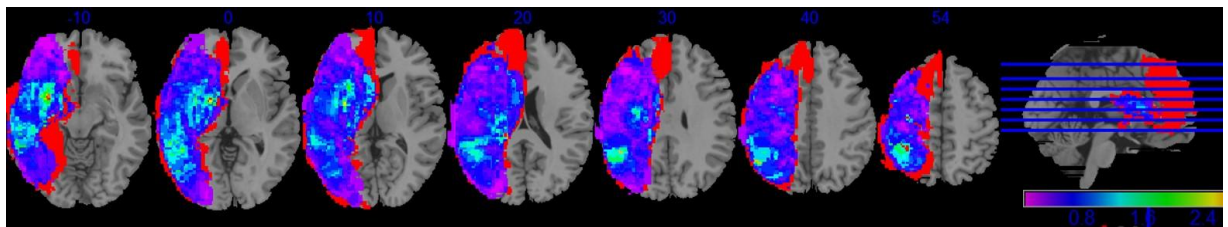


Figure 1. Lesion patterns associated with Complex regional pain syndrome (CRPS). Voxel based lesion symptom mapping analysis shows the relationship between presence of CRPS and brain lesions.