Functional Magnetic Resonance Imaging and Diffusion Tensor Imaging in a Case of Central Poststroke Pain

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Abstract: **The role of the lesion location within functional pain systems is not fully understood for central poststroke pain (CPSP) pathogenesis. In a patient with CPSP we used data from both functional magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) for anatomo-functional correlations. Structural MRI showed a small residual cavity confined to the right thalamic ventral posterolateral nucleus and the adjacent posterior arm of the internal capsule. DTI maps showed selective reduction of right sensory thalamocortical fibers. Functional MRI, performed with different thermonociceptive stimuli, showed pain-specific signal changes in the anterior cingulate gyrus (BA 24/32) and in the associative parietal regions (BA 5/7). These findings underline, for CPSP pathogenesis, the role of damage of lateral nociceptive thalamoparietal fibers together with the release of activity of anterior cingulate and posterior parietal regions.**

Perspective: ***In a patient with CPSP, we combined noninvasive neuroimaging techniques (functional and diffusion MRI) to assess the anatomo-functional relationship in CPSP. Our investigations show, for CPSP pathogenesis, the role of damage of lateral nociceptive thalamoparietal fibers together with the release of activity of anterior cingulate and posterior parietal regions.***

Key words: *Central pain, allodynia, diffusion MRI, functional MRI, thalamocortical fibers.*

The development of neuropathic pain after stroke is not uncommon and has severe consequences on functional recovery. Central poststroke pain (CPSP) can be defined as a neuropathic pain syndrome occurring after stroke, in which the patient experiences constant or intermittent pain on the affected side of the body with associated sensory abnormalities.[2,6] This syndrome, initially associated with thalamic involvement, might be the consequence of stroke in several extrathalamic sites[7] situated along the spinothalamic and sensory thalamocortical pathways.

Functional neuroimaging studies on healthy subjects[5,9,12,21] pointed to the role of the cingulate gyrus, insula, dorsolateral prefrontal cortex, secondary somatosensory cortex, inferior parietal lobe, cerebellum, and lateral thalamus in central pain processing. The same brain regions appear to be globally involved in the pathogenesis of CPSP,[14,15,17,20] but the exact role of the lesion within the pain processing systems is not fully understood. In this context, not surprisingly, the treatment of CPSP remains a particularly challenging task.

In a patient with CPSP we attempted to use data from functional MRI (fMRI) and diffusion tensor imaging (DTI) to study the effect of the lesion within pain functional systems. The combination of fMRI and DTI techniques allows the assessment of the anatomo-functional correlates of the CPSP. This combination showed an extensive loss of lateral thalamocortical fibers associated with increased activity in the anterior cingulate gyrus and posterior parietal regions.

Material and Methods

Case Report

A 65-year-old right-handed man had suffered a hypertensive hemorrhagic stroke in 1997, which resulted in dense left hypoesthesia and hemiplegia, as well as in executive and memory dysfunction. During the first 3 months after stroke, the patient exhibited significant

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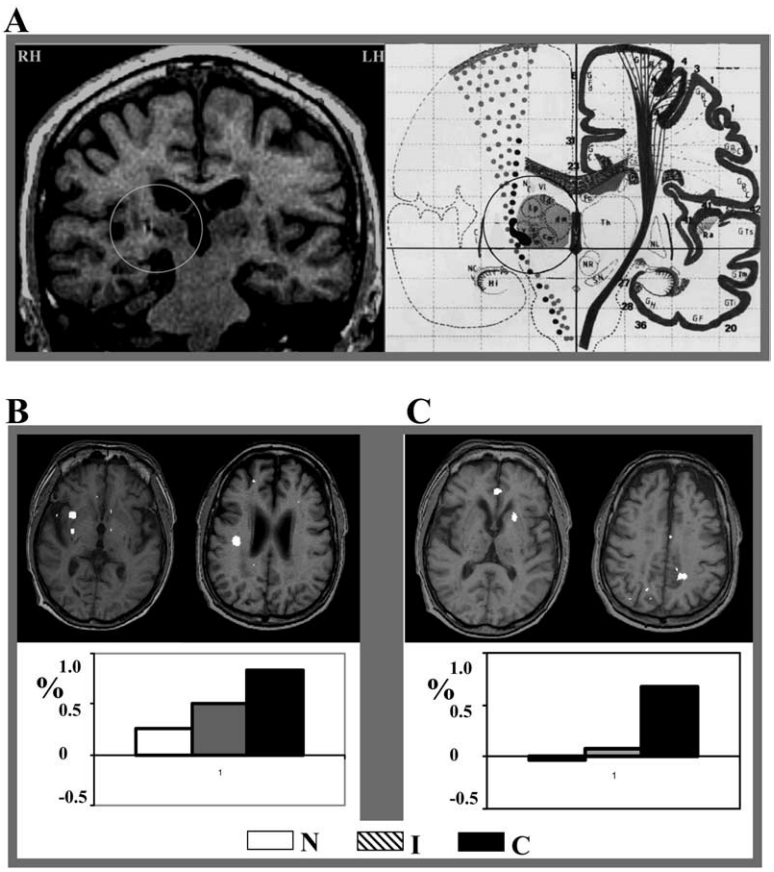

Figure 1. **A**, Coronal section of the anatomic volume of the patient and a schematic figure based on the Talairach template (at the corresponding y-plane = –20), which indicates the relative localization of the lesion (delimited by a circle). **B**, Functional activation maps showing (in white clusters) temperature-related responses in the middle insula and the mesial postcentral gyrus in the right hemisphere, activated when stimulating the left hand with decreasing stimulus temperature, and their percent signal changes during each of the 3 conditions. **C**, Functional activation maps showing (in white clusters) the anterior cingulate cortex (BA 24/32), left putamen, and left associative parietal cortex (BA 5/7) activated in the painful condition (cold stimulation of the left hand), and their percent signal changes during each of the 3 conditions.

neurologic and functional improvements on cognitive and motor functions. His residual deficits included a severe left thermoalgic and mild tactile, proprioceptive hypoesthesia, cerebellar ataxia, and decreased verbal/figural fluency. Functional autonomy was satisfactory (functional independence measure score, 116/126). Four months after stroke, progressively during a few weeks, he developed a deep and superficial burning cold-like pain in his left body, more pronounced on the pectoral region, hand, and foot. The pain was constant with an intensity varying from 50/100 to 70/100 points on a visual analog scale but had frequent paroxysms. Trigger stimuli were "unattended" touches, contact with cold objects, and being in cool environments. Pain aggravation during winter 2001 rendered the patient unable to walk because the contact of his left foot with the ground became severely painful. Clinical examinations showed severe left hypesthesia for heat (37°C to 42°C), warm (33°C), and cold (6°C to 10°C) temperatures, selective allodynia for cold stimuli (<6°C), and pinprick hyperpathia. Spontaneous pain, allodynia, and hyperpathia had an exquisite cold burning quality. Structural brain MRI showed a residual hemorrhagic cavity in the ventral posterolateral nucleus (VPL)[18] of the right thalamus and in the adjacent posterior third of the posterior arm of the internal capsule (Fig 1, *A*). Talairach coordinates[23] of the center of the lesion were x y z = +26 –18 +2.

During the following 6 months, treatment with gabapentin, amitriptyline, and fluoxetine, with doses progressively increased up to 2400, 75, and 20 mg per day, respectively, induced a significant improvement (about 40% reduction) on the constant, paroxysmal, and affective components of pain. At that time, informed consent was obtained from the patient to undergo our combined DTI-fMRI study. This study was approved by the ethical committee of the Geneva University Hospitals. All experiments were performed on a 1.5T INTERA system (Philips Medical Systems, Best, The Netherlands).

DTI Acquisition and Processing

An SE-EPI sequence (field of view, 200 mm; echo time, 65 milliseconds; b-factor, 1000 s/mm^2; 6 noncollinear directions; 27 contiguous 5-mm slices) was used. The acquisition was repeated 2 times to improve the signal-to-noise ratio. The total time for DTI acquisition was about 3 minutes.