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ORIGINAL ARTICLE/ARTICLE ORIGINAL

# Central representation of the RIII flexion reflex associated with overt motor reaction: An fMRI study

# Représentation centrale de la réponse motrice (retrait) à la douleur. Une étude IRMf du réflexe nociceptif en flexion (RIII)

**R. Peyron[a,d,*], R. Kupers[b], J.L. Jehl[a], L. Garcia-Larrea[d], P. Convers[a,d], F.G. Barral[c], B. Laurent[a,d]**

[a] *Département de neurologie, CHU de St-Étienne, 42055 St-Étienne, France*
[b] *PET Center and Department Surgical Pathophysiology, Rigshospitalet, Copenhagen, Denmark*
[c] *Département de neuroradiologie, CHU de St-Étienne, 42055 St-Étienne, France*
[d] *Inserm EMI0342, Lyon, UCB Lyon-1 and UJM St-Étienne, St-Étienne, France*

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**Summary** Recent neuroimaging studies precised the functions of the brain regions included in the so-called ''pain-matrix''. They isolated brain structures mediating attentional, emotional, anticipatory, cognitive, and discriminative aspects of pain perception. Surprisingly, little attention was devoted to isolate the cerebral network associated with the motor response to pain. In this study, we used fMRI to measure BOLD signal changes in nine volunteers while they received low- (L-) and high- (H-) intensity painful electrical shocks on the (left) lower limb. High-intensity stimulation was associated with a significantly stronger pain sensation and with a pronounced motor (withdrawal) reflex. BOLD responses common to L- and H-stimulation intensities were found in the right prefrontal and right posterior parietal cortices. These did not correlate with subjective pain ratings and probably mediate attentional processes unrelated to pain intensity and withdrawal. In contrast, signal changes in insula, left SII cortices and right amygdala did correlate with pain ratings and are therefore likely to encode for pain intensity. High-intensity shocks selectively recruited a motor network, including vermis, MI, SI, and paracentral cortices bilaterally, right premotor, right SII and posterior cingulate cortices. These responses, assessed for the first time in a functional imaging study, emphazised on the presence of a motor component in what has been described as the pain-matrix. They should be considered as a motor component of pain-related processes activated in case of intense pain.


* Corresponding author.
*E-mail address:* Roland.Peyron@univ-st-etienne.fr (R. Peyron).

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**MOTS CLÉS**
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RIII ;
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Homme ;
Motricité

**Résumé** Les réponses cérébrales à la douleur étudiées en imagerie fonctionnelle comportent des composantes attentionnelles, anticipatoires, discriminatives ou émotionnelles dont les représentations corticales ont été largement étudiées. En revanche, les réponses corticales associées à la riposte motrice face à une stimulation douloureuse n'ont suscité que peu d'études chez l'homme. Nous avons utilisé l'IRM fonctionnelle (IRMf) pour étudier ces réponses, chez neuf volontaires, soumis à des stimulations électriques phasiques, alternativement de forte et de très forte intensité sur le membre inférieur gauche. Les stimulations très fortes étaient perçues comme plus douloureuses et induisaient un réflexe de retrait plus important que les intensités fortes. Les réponses communes aux fortes et aux très fortes intensités de stimulation, concernaient le cortex pré-frontal et postérieur pariétal droit. Ces activités non corrélées avec la perception douloureuse subjective, gèrent vraisemblablement les processus attentionnels, indépendants de l'intensité de la douleur et de la réponse de retrait. En revanche, les modifications de signal BOLD dans les insulae, le cortex SII à gauche et l'amygdale droite sont corrélées de manière linéaire à la cotation douloureuse et encodent donc vraisemblablement l'intensité de la perception douloureuse. Les très fortes intensités de stimulation recrutent un réseau moteur, comportant le cortex moteur primaire, SI et le cortex paracentral bilatéralement, le vermis, le cortex pré-moteur droit, SII droit et le cortex cingulaire postérieur. Ces réponses soulignent la participation des activités motrices dans ce qu'il est convenu d'appeler la matrice douleur. Ces activités peuvent être considérées comme la composante motrice de la douleur, associée à un retrait, en particulier lors de douleur très intense.


## Introduction

Already in 1968, Melzack and Casey [1] proposed that pain is a subjective and multidimensional experience that consists of sensory-discriminative, motivational, and cognitive aspects. Neuroimaging studies over the past decade have provided ample evidence supporting this view and have focussed extensively on how affective, anticipatory, attentional, discriminative, or cognitive processes do modulate neuronal activity in the pain-matrix. Brain regions involved in motor functions such as primary motor (MI) and premotor cortex, supplementary motor area (SMA), anterior cingulate (ACC), and cerebellum are considered to be part of the pain-matrix. Nonetheless, surprisingly little attention has been devoted to isolate the cerebral correlates of the reflex motor activity concomitant with pain. In the vast majority of pain imaging studies, both experimental procedures and instructions to volunteers concur to suppress pain-induced movements. To avoid motion artifacts and activations related to motor responses, subjects are asked to lay still and not to move (withdraw) as the noxious stimulus is applied. This is at odds with daily life situations, in which pain automatically induces spontaneous, reflex-like withdrawal responses.

Studying pain-related motor functions requires that the experiment separates pain from the cerebral correlate of the reflex motor activity. A first indirect attempt in this direction was done by comparing the cerebral correlates of the motor response during unpleasant itch. In this condition, the motor intention of the urge to scratch represents the motor action associated with an unpleasant sensation and involves the premotor cortical areas, SMA, and inferior parietal lobule [2]. In restless leg syndrome, another situation associating discomfort and motor movements, activation was found in cerebellum, thalamus, red nucleus, and brainstem [3]. A later study explored the cerebral correlates of the pain-related RIII withdrawal (flexion) reflex [4]. However, this study failed to detect activity in areas that are considered to be part of the pain-matrix.

Except for these three early attempts, there is only one other study that tried to single out the pain-associated motor component [5] in the whole brain. This study investigated the motor pattern that was involved in the manual scoring of pain intensity immediately after a noxious stimulus had been applied. This experimental situation differs fundamentally from the natural motor reaction to pain and introduce a confounding variable, which is temporally dissociated from pain and related to the voluntary motor action. Another theoretical possibility would be to study subjects while they mimic a withdrawal movement, a situation that would also introduce a confounding component related to voluntary motor action, whose presence would minimize the relevance of the insight into pain processes.

In this study, we applied phasic electrical stimuli and asked subjects not to suppress their motor responses, if any, to the noxious stimulation. This allowed us exploring not only the subjective responses to pain, as in previous experiments, but also, simultaneously, the intrinsically associated spontaneous withdrawal response, which is usually contained owing to the instructions given to subjects.

## Material and methods

### Subjects

Nine healthy right-handed male volunteers (mean age $19.9 \pm 1.1$ year) without known neuropsychiatric disorders participated in the study. Subjects were asked to refrain from analgesic intake during the week preceding the study. The study protocol was approved by the local ethics committee (St-Étienne, France) and subjects provided written informed consent.