

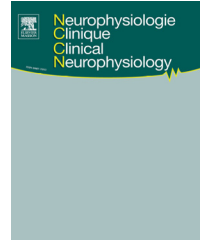


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ORIGINAL ARTICLE/ARTICLE ORIGINAL

# Peripheral sensitization reduces laser-evoked potential habituation



## *Réduction de l'habituation des potentiels évoqués au laser par la sensibilisation périphérique*

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### KEYWORDS

Capsaicin;  
Laser-evoked potentials;  
Peripheral sensitization;  
Central sensitization;  
Central habituation;  
Quantitative sensory testing

### Summary

**Objective.** – Laser-evoked potential (LEP) habituation was investigated under the influence of capsaicin-induced peripheral and central sensitization.

**Material and methods.** – Fifteen subjects received 100 repetitive painful laser stimuli at the right hand dorsum at primary (application area; condition I) and secondary areas (beyond application area; condition II) in two different sessions after applying capsaicin topically. Conditions I and II were compared to a control condition without capsaicin application. N1, N2, and P2 latencies and N1 and N2/P2 amplitudes were recorded by EEG. Quantitative sensory testing (QST) and the Liewald Diary reaction time experiment were used as control tests.

**Results.** – QST documented heat hyperalgesia as a sign of peripheral sensitization in the primary area and pinprick hyperalgesia in the primary and secondary area as a sign of central sensitization, after applying capsaicin. The N2/P2 amplitude habituation was significantly reduced in the primary area compared to controls (the primary area represents peripheral sensitization). The LEPs of the secondary area (the secondary area represents central sensitization) showed no significant N2/P2 amplitude habituation compared to controls. The comparison between conditions I vs. II showed no significant difference regarding N2/P2 amplitude and laser pain rating.

**Conclusion.** – Capsaicin-induced central sensitization does not alter LEP habituation. The physiological habituation of LEP amplitudes is reduced due to peripheral mechanisms after applying

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**MOTS CLÉS**

Capsaïcine ;  
 Potentiels évoqués au laser ;  
 Sensibilisation périphérique ;  
 Sensibilisation centrale ;  
 Habituation centrale ;  
 Tests sensoriels quantitatifs

capsaicin topically. These findings form a basis for future studies, which use the habituation paradigm to investigate pain conditions promoted by sensitization phenomena.

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**Résumé**

*Objectif.* – L’habituation des potentiels évoqués au laser (PEL) a été étudiée sous l’influence de la sensibilisation périphérique et centrale induite par la capsaïcine.

*Matériel et méthode.* – Quinze sujets ont reçu 100 stimuli laser douloureux sur le dos de la main droite, dans une zone primaire (zone d’application; condition I) puis secondaire (hors de la zone d’application ; condition II) en deux étapes différentes, après application topique de la capsaïcine. Les conditions I et II ont été comparées à des contrôles sans application de capsaïcine. Les latences N1, N2 et P2 et les amplitudes N1 et N2/P2 ont été enregistrées par EEG. Comme tests de contrôle on a effectué des tests sensoriels quantitatifs (QST) et mesuré le temps de réaction de Liewald Diary.

*Résultats.* – Les QST ont permis de mettre en évidence une hyperalgésie à la chaleur, signe de sensibilisation périphérique dans la zone primaire, et une hyperalgésie aux pincements dans les zones primaires et secondaires, considérée comme signe de sensibilisation centrale, après application de la capsaïcine. L’habituation de l’amplitude N2/P2 était significativement réduite dans la zone primaire en comparaison des contrôles (les zones primaires représentant une sensibilisation périphérique). Aucune différence significative de l’habituation à l’amplitude N2/P2 en comparaison des conditions contrôle n’a pu être mise en évidence pour les PEL de la zone secondaire (les zones secondaires représentant la sensibilisation centrale). Aucune différence significative n’a pu être mise en évidence entre les conditions I et II.

*Conclusion.* – La sensibilisation centrale induite par la capsaïcine ne modifie pas l’habituation à la PEL. L’habituation physiologique de l’amplitude des PEL est réduite par des mécanismes périphériques après application topique de la capsaïcine. Ces observations représentent une base de travail pour de futures études, dans lesquelles le paradigme de l’habituation pourra être utilisé pour étudier les conditions de douleur provoquées par des phénomènes de sensibilisation.

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**Introduction**

Repetitive laser stimulation reproducibly induces laser-evoked potential habituation, i.e., a decrement in N2/P2 amplitudes and laser pain rating [6–8,16,32]. In migraine and fibromyalgia patients [6,7] N2/P2 habituation is diminished, which indicates altered central pain processing and central sensitization. It is likely that other chronic pain conditions, which are characterized by central sensitization (e.g. neuropathic pain), also show diminished LEP habituation. To address this question we used an established surrogate model of central sensitization, i.e. the capsaicin surrogate model [3,15,28]. Topically applied capsaicin induces heat hyperalgesia in the application area (primary area), which is due to peripheral sensitization. Pinprick hyperalgesia develops within minutes after applying capsaicin in the primary area and the surrounding secondary area [3,17,19], as a result of central sensitization phenomena [1,21,34].

We hypothesized that topical application of capsaicin would reduce N2/P2 LEP habituation. To distinguish whether habituation is reduced by peripheral or central sensitization mechanisms, 100 painful laser stimuli were applied and recorded in the primary application area (condition I) and the secondary area (condition II).

**Material and methods**

LEP habituation was tested in healthy subjects by applying 100 painful laser stimuli at the dorsum of the right hand [16]. LEPs were averaged block-wise with 25 stimuli per block, so that the time course of habituation could be documented (i.e. 4 blocks). The time course of habituation was investigated under three sets of conditions:

- condition I: LEPs were performed in the primary area after applying capsaicin topically at the dorsum of the right hand ( $n = 15$ , 4 male, 11 female, age  $23.4 \pm 1.7$  years);
- condition II: LEPs were performed in the secondary area (beyond the application area) after applying capsaicin topically at the dorsum of the right hand;
- capsaicin Controls: LEPs (4 blocks of 25 stimuli each) were performed at the dorsum of the right hand without applying capsaicin, to document the normal uninfluenced time course of LEP habituation.

The test sessions were performed on different days in the laboratory with at least two weeks between each condition (two weeks were chosen to minimize memory effects). The order of the test sessions was randomized. The subjects were told that the small-fiber activity was being tested

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