# Characterization of non-evoked pain after a surgical incision

B. Pfleiderer[1], A. Meinhardt[2], C. Wagner[2], P. K. Zahn[2], E. Pogatzki-Zahn[2]

[1]Department of Clinical Radiology, University Hospital Münster, Münster, NRW, Germany, [2]Department of Anesthesiology, University Hospital Münster, Münster, NRW, Germany

## Introduction

There is ample evidence that different brain regions like thalamus, somatosensory cortex (S1, S2), insula and cingulate cortex are involved in experimental nociceptive pain. However little is known about cortical activation and the functional significance of distinct brain regions after pain caused by models of experimental tissue injury like postoperative pain. Postoperative, incisional pain is an unique but common form of acute pain. Therefore a model for postoperative pain in animals and healthy human volunteers (Kawamata et al 2002) has been developed and characterized. In the present study, we examined for the first time the activation of different brain areas after an experimental surgical incision (based on Kawamata et al 2002) and the pathophysiological role of distinct cortical activation for non-evoked pain to mechanical stimuli caused by an incision.

## Methods

***Study design:*** 44 healthy, male human volunteers (25.1 ± 5J, right-handed) were investigated. 30 volunteers (25 +/- 5 years) received an experimental incision (4 mm) within the anterior aspect of the right forearm using a number 11 ceramic scalper blade; 14 volunteers (25 +/- 4 years) received a sham procedure. Images were taken (block design) before, during (0-4.5 min) and after incision/sham procedure (4.5-10 min, 24-29 min, 44-49 min; Fig. 1). Psychophysics were performed between the scans.

***Imaguing***: fMRI Images were taken on a 3T (Gyroscan, Intera, Philips, Best, NL) scanner. MRI-protocol: 312 GE-EPI-volumes, matrix: 64x64, FOV=210 mm, 36 oblique slices, slice thickness = 3.6 mm, TE = 35 ms, TR = 3 sec, scan duration = 1.67 sec.

***Psychophysical tests:*** Subjects were asked to rate the intensity of *non-evoked pain* on a numerical rating scale (NRS) ranging from 0 ("no pain") to 100 ("worst pain imaginable"; for results see Fig. 2). To determine *primary hyperalgesia*, seven von Frey filaments (15 to 142mN) were applied adjacent to the incision. Each filament was applied once starting with the lowest filament (15mN) until pain or pricking was reported by the volunteer. The median force of the three trials was defined as the punctuate mechanical pain threshold. If the filament with the greatest bending force did not lead to a painful sensation, 198mN was assigned as the pain threshold.

***Data analysis:*** Image Processing and statistical analysis of the fMRI images were done by SPM2 first and second level standard routines and templates (www.fil.ion.ucl.ac.uk/spm) and SPSS 12.0.

## Results and discussion

Distinct brain areas are activated by an experimental incision.Similar to other studies the somatosensory cortex and the limbic system were also activated. A distinct temporal profile of activity within specific brain regions occurred after incision: starting with 2 min after incision an increasing activation of the limbic system (BA23/24) was observed. During incision (0-2 min) there was an exclusive and significant activity of frontal brain regions (BA 6, 7, 8, 9 (see Fig. 3)); these areas are responsible for the assessment of pain intensity. Peak brain activity occurred 4.5-10 min after incision and subsequently neuronal activity decreased. 44-49 min after incision, no differences in brain activity were observed compared to sham incision. There was a strong correlation 0-10 min after incision between non-evoked pain ratings during incision and ventrolateral thalamus activation (second level, spm2, p = 0.005). 24-29 min after incision a correlation with NRS pain scores (20min) and mainly frontal brain areas (contralateral BA 6-9) was found. Our data indicate an important role of distinct brain areas for the development of non-evoked pain after incision

**Figure 1:**

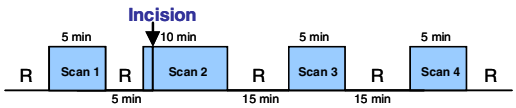


**Figure 2:**

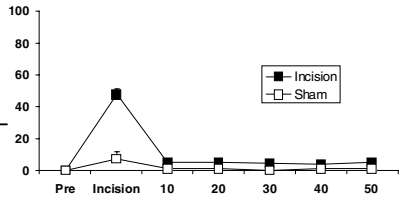


**Figure 3:**

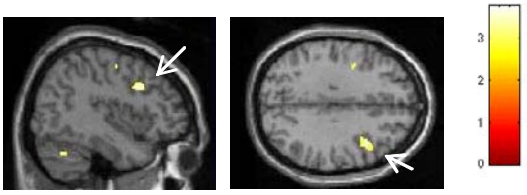


*Fig.1:* ***Study design: MRI cans were performed before (baseline, 1min before incision), during (0-2 min) and after (2-4.5, 4.5-10 min, 24-29 min, 44-49 min. Between MRI-Scans (R = rest), psychophysical tests were carried out (see text).*** *Fig. 2: Non-evoked pain (NRS 0-100 before, during and after incision and sham procedure. Results are expressed as mean + standard error of the mean (SEM)). Fig. 3: Activation 2 min after incision: BA 9 (i (arrow), c) incision > sham, 2 sample t-test, T = 3.4. uncorrected, 4 voxels.*

Kawamata, M., Takahashi, T., Kozuka, Y., Nawa, Y., Nishikawa, K., Narimatsu, E., Watanabe, H. and Namiki, A., Pain, 100 (2002) 77-89.