loop adjusted the laser power. 8 subjects participated in this study. Stimulations were applied on the dorsum side and in the palm of the hand. Subjects were instructed to continuously rate the pain intensity. First the subject was stimulated using both a rising 35–45 °C staircase and a decreasing 45–35 °C staircase in both skin types; each staircase step was 1 °C and lasted for 15 s. Offset analgesia was tested by stimulating the hairy skin on the dorsum of the hand using two sequential temperature plateaus (48–48 °C, 48–49 °C, 49–48 °C and 49–49 °C). Each plateau was held for 5 s.

Results: For the staircase stimulations identical surface temperatures were perceived significantly higher in glabrous than in hairy skin ($p < 0.001$). The offset analgesia test showed that a decrease in temperature from 49 to 48 °C evoked a drop in the pain rating which was significantly lower than observed during a 48–48 °C stimulation ($p < 0.001$) indicating offset analgesia.

Conclusion: A non-contact thermal stimulator is able to evoke offset analgesia. Furthermore, it was noted that a high penetration laser causes higher pain ratings in glabrous skin than in hairy skin—a relationship which is opposite to low penetration lasers (CO_2 laser) and contact heat stimulation.

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Inhibition of FAAH reverses spinal LTP

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Objectives: Fatty-acid amide hydrolase (FAAH) is an enzyme that metabolizes several endocannabinoids and fatty acid amides important for human pain sensitivity. Here we examine how reduced FAAH activity affects maintenance of spinal long-term potentiation (LTP) and spinal expression of the transcription factor Zif.

Methods: Dorsal horn field potential recordings were performed in urethane anaesthetized SPD rats. LTP was induced by high frequency stimulation (HFS) conditioning applied to the sciatic nerve. To inhibit the enzymatic activity of FAAH, URB 597 was administered (1 mg/kg i.v.). Gene expression of the transcription factor Zif was examined by real time RT-PCR.

Results: A clear LTP was observed after HFS conditioning. The expression of LTP was, however, significantly reduced after i.v. administration of the FAAH inhibitor URB 597. A significant increase in the gene expression level of Zif was demonstrated in the ipsilateral dorsal horn after HFS compared to the corresponding control.

Conclusion: Our results demonstrated that inhibition of FAAH partly reverses spinal LTP. While the HFS conditioning caused a clear increase in Zif gene expression in the ipsilateral dorsal horn, HFS in combination with the FAAH inhibitor did not. We conclude that FAAH may be important for the neuronal mechanisms underlying maintenance of spinal LTP. Whether or not the increased gene expression of Zif is important for these mechanisms remains to be investigated.

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Hyperexcitable C-nociceptors in human paroxysmal pain

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Objectives: Spontaneously occurring paroxysmal pain is an important constituent of the symptomatology of neuropathic pain. While mechanisms of stimulus-evoked pain and also spontaneous ongoing pain have been studied for a long time, little emphasis has been put on the mechanisms of paroxysmal pain. The objective of the present study was to record from single C-nociceptive fibres in a patient presenting with pure paroxysmal pain.

Methods: A woman diagnosed with Ehler-Danlos syndrome was investigated clinically in two separate sessions with 1–2 years apart as well as with EMG/neurography, QST (assessment of thermal thresholds), QSART (quantitative sudomotor axon reflex test) and microneurography.

Results: At the time of the first investigation, the patient reported only spontaneous paroxysmal pain of high intensity several times daily, appearing all over the body. One–two years later the paroxysmal pain was unaltered, but she had during the last months developed an ongoing pain in the feet. On both occasions EMG/neurography and QSART were normal, whereas thermal thresholds on the dorsum of the feet were highly elevated. Microneurography from 29 C-nociceptive fibres showed a high amount of fibres with signs of hyperexcitability (spontaneous activity and sensitisation for mechanical stimulation).

Conclusion: Although the relationship between spontaneous paroxysmal pain, spontaneous ongoing pain and hyperexcitable peripheral C-nociceptors are unclear, the findings in this patient could represent an interesting contribution to the understanding of mechanisms underlying spontaneous paroxysmal pain.

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Pain sensitivity and experimentally induced sensitization in red haired women

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Pain sensitivity has been linked to the melanocortin-1 receptor (MC1R) gene. A mutation in MC1R can result in pale skin and red hair in humans. The aim of this study was to investigate pain sensitivity in redheads. Twenty healthy women with pale skin and red hair (mean age 32 years, range 20–55) and 20 healthy women with blond/dark hair (mean age 31 years, range 20–51) participated in this study. On the left arm pain tolerance threshold to heat and pressure stimulation was determined. On the right arm 0.075% topical capsaicin cream was applied for 30 min. Thereafter the secondary hyperalgesic area was estimated with a calibrated filament (von Frey hair, 15 g) and the allodynic area by a soft brush. This was done 0, 30, 60 and 90 min after removing the cream. There was no difference in either heat or pressure pain tolerance thresholds between the two groups (heat: $P = 0.8$; pressure: $P = 1.0$). The areas to pinprick were significantly smaller for red haired women than non-red haired women ($P = 0.014$). There were no significantly differences in the allodynic areas. Redheads were less sensitive to capsaicin induced hyperalgesia compared to non-redheads which could

be a manifestation of central anti-hyperalgesic involvement of MCR's.

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How are opioids used in Norway? Persistent use, utilization of depot formulation and age profile in non-palliation patients

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Objectives: The extent of persistent opioid use in Norway is unknown. We have studied how many persistent opioid users there are in Norway, whether they use long- or short acting opioids and the age distribution of these patients.
Methods: We have used the Norwegian prescription database containing all drugs dispensed since 2004. We have created three definitions of persistent opioid use corresponding to different clinical settings. The tree definitions are based on amount of opioid dispensed, frequency of dispensing and distribution of dispensing throughout the year. We will present 2008 data of non cancer patients. These three patient groups are: (1) Wide: opioids are used on and off throughout the year in at least half the days. (2) Intermediary: opioids are used on average every day throughout the year. (3) Strict: opioids are used continuously every day in high doses throughout the year.
Results: There are 421,724 non-persistent opioid users in 2008. There are 24,462, 14,132 and 6547 in settings 1, 2 and 3 respectively. These numbers account for 8.90, 0.52, 0.30 and 0.14% of the Norwegian population. Together the three groups of patients account for 45,141 persistent opioid users (0.95% of the population). The percentage of users who use mainly long acting opioids (>80%) is; 2.7%, 9.7%, 16.0% and 36.9% for non-persistent users, groups 1, 2 and 3 respectively. The age of opioid users was studied. The percentage under 30 years old was 14.6%, 2.3%, 2.1% and 3.3% for non-persistent users and groups 1, 2 and 3 respectively. Over 60 years old the percentages are 36.0%, 53.0%, 46.1% and 33.1% respectively.
Conclusion: Less than 10% of people using opioids in 2008 are persistent users. Young people use opioids less persistently. There is a correlation between increased degree of persistence and increased use of long acting opioids.

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To which extent does incident and persistent use of weak opioids predict problematic opioid use?

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Background: A high consumption of weak opioids may contribute to prescription abuse of opioids, but the risk of development of problematic opioid use in patients starting opioid therapy is not established.
Objective: To investigate the prevalence of prescription patterns indicating problematic opioid use in a cohort of patients starting therapy with the weak opioids.
Materials and methods: Prescription data were drawn from the nationwide Norwegian Prescription Database. The study population (N = 243,228) consisted of all adult patients in Norway receiving one or more dispensions of the weak opioids codeine and tramadol in 2005, who had not received any opioid in 2004. This cohort was followed until December 2008 and their dispensions of opioids and benzodiazepines during the study period were investigated, with focus on the patients who received opioid dispensions each year during the study period. Problematic opioid use patients had to meet the following three criteria: dispensed more than 365 defined daily doses (DDDs) of opioids, receiving prescriptions from more than three doctors and were dispensed more than 100 DDDs of benzodiazepines during 2008.
Results: In 2005 there were 243,228 new users of weak opioids (216,902 of codeine, 26,326 of tramadol) representing 5% of the Norwegian population. 17,005 (7%) received opioids every year during the study period 2005–2008. About 4% (N = 669) of the subjects who received opioids every year were dispensed >365 DDDs opioids in 2008 and 31% (N = 5328) co-medicated with benzodiazepines. 182 subjects were classified as possible problematic opioid users.
Conclusion: Among new users of weak opioids in 2005, 7% continued to receive one or more prescription of weak opioids the three following years. However, only 0.07% of the cohort starting weak opioids in 2005 developed a prescription pattern during four years of follow-up which indicates problematic opioid use.

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Is transdermal buprenorphine for chronic non-malignant pain used long term without co-medication with other potentially addictive drugs?

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Objectives: Guidelines for the appropriate use of opioids to patients with persistent non-cancer pain recommend the use of long-acting opioids. Low dose transdermal buprenorphine (LD-TD-BUP) was introduced as the first depot opioid designed specifically to be used long term to patients with chronic non-malignant pain. Primary aim was to see how many patients prescribed LD-TD-BUP would become long-term users for non-malignant pain. Secondary aim was to see how many patients co-medicated with opioids or other potentially addictive drugs.
Methods: Data were drawn from the Norwegian prescription Data Base (NorPD), which covers all prescriptions dispensed to the entire population. Reimbursements codes are also recorded making it possible to differentiate between prescriptions for cancer pain and non-malignant pain.
We define the study population as all patients who were dispensed at least one prescription of LD-TD-BUP during the study period 2006–2008. Patients who were dispensed more than 24 patches (≥6 months) were defined as long-term users. Co-medication with opioids or other potential addictive drugs during the same period were included in the analyses.