tions between the degree of neuroma formation and the docking length. We examined effects of docking length on behaviour of piglets during and 6 h after tail docking.

Methods: Piglets were tail docked 2–4 d post-partum. We used 53 piglets and four treatments: intact (I), removal of either 25 (Q), 50 (H) or 75% (T) of the tail. The piglets were kept with sow and littermates under production conditions, and docked using a gas-heated instrument. Behaviour was observed during docking and for the following 6 h.

Results: Tail docking led to behavioural changes, the magnitude of which to some extend depended on docking length. Increased docking length led to increased intra-procedural vocalization score (0, 0.6 ± 0.2, 1.4 ± 0.2 and 1.4 ± 0.2 for I, Q, H and T, respectively, $P < 0.001$). In the initial 6 h, increased docking length led to increased time spent in the heated creep area ($2 \pm 1\%$, $15 \pm 6\%$, $18 \pm 8\%$ and $30 \pm 6\%$ for I, Q, H and T, respectively; $P < 0.05$). Piglet posture was affected as well, showing that increased docking length led to decreased lying ($71 \pm 2\%$, $68 \pm 2\%$, $61 \pm 2\%$ and $61 \pm 2\%$ for I, Q, H and T, respectively, $P < 0.01$) and increased time spent active ($24 \pm 2\%$, $23 \pm 2\%$, $32 \pm 2\%$ and $30 \pm 3\%$ for I, Q, H and T, respectively, $P < 0.05$). Pain specific behaviours such as trembling or tail flicking were registered and occurred in $5 \pm 1\%$ and $9 \pm 1\%$ of observations. However, no effects of docking length could be shown.

Conclusions: Piglets responded behaviourally to tail docking. Increasing docking length led to increased pain responses such as intra-procedural vocalizations, hiding behaviour and reduced rest, indicative of increased pain. These results confirm earlier reports suggesting that tail docking might be suitable as an animal model for neuropathy and pain.

http://dx.doi.org/10.1016/j.sjpain.2012.05.034

T5

Dose and administration-period play a key role in the effect of ceftriaxone on neuropathic pain in CCI-operated rats

K.K. Frederiksen, P. Kristensen, P.H. Honoré, G. Gegelashvili, O.J. Bjerrum*

Department of Drug Design and Pharmacotherapy, University of Copenhagen, Copenhagen, Denmark

Introduction: An unmet medical need for more effective therapies of neuropathic pain exits. Here modulation of the glutaminergic system represents an unexplored possibility. Down-regulation of glutamate transporters potentiates pain transmission by delaying the removal of glutamate from the synapse. In the spinal cord, glutamate transporter 1 (GLT-1) is responsible for more than 90% of the glutamate uptake. Ceftriaxone, a β-lactam, is believed to induce the expression of GLT-1 through the transcriptional factor (NF-κB) pathway, which results in induced promoter activity and thereby increased synthesis of GLT-1 protein.

Objectives: To evaluate the analgesic effect of ceftriaxone in the Chronic Constriction Injury (CCI) rat model of neuropathic pain and to investigate the pharmacodynamics of ceftriaxone in a chronic dosing regime.

Methods: In CCI rats, mechanical and thermal hypersensitivity, were determined with von Frey filaments and Hargreaves test, respectively. Groups of rats received ceftriaxone (200, 300 or 400 mg/kg, i.p.) once daily in 7–19 days and the control groups received vehicle.

Results: From a total of 24 CCI operated rats, 16 rats developed both mechanical (withdrawal threshold ≤ 3 g) and thermal hypersensitivity (latency threshold ≤ 13 s.). Ceftriaxone alleviated mechanical allodynia and thermal hyperalgesia in CCI operated. Daily dosing of ceftriaxone 200, 300 and 400 mg/kg reached the same withdrawal threshold levels as before the CCI surgery, after 18, 12 and 7 days, respectively. This indicates that the dynamic effect of ceftriaxone is not only dependent of the dose, but also the duration of administration. Thus, it seems that dose exposure above a certain threshold is necessary to induce protein synthesis.

Conclusion: The CCI model is a useful model to evaluate the anti-nociceptive effects of ceftriaxone. Increased dose do not only elevate effect magnitude but also the rate of with which the effect appears.

http://dx.doi.org/10.1016/j.sjpain.2012.05.035

T6

Translational aspects of rectal evoked potentials: A comparative study in rats and humans

Thomas Dahl Nissen[1,2,3,*], Carina Graversen[1], Steven Coen[4], Leif Hultin[3], Qasim Aziz[4], Jens Lykkesfeldt[2], Asbjørn Mohr Drewes[1], Christina Brock[1]

[1] *Mech-Sense, Department of Gastroenterology & Hepatology, Aalborg Hospital, Aarhus University Hospital, Denmark*
[2] *Section of Biomedicine, Department of Veterinary Disease Biology, Faculty of Life Sciences, University of Copenhagen, Denmark*
[3] *Bioscience, AstraZeneca R&D, Mölndal, Sweden*
[4] *Wingate Institute of Neurogastroenterology, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, England, United Kingdom*

Background: In recent years only few novel drugs targeting visceral pain have been developed. This lack of success may be explained by animal models having poor predictive value. To increase the success of translating results from animals to humans there is a demand for comparable test models. The aim was to establish a comparable and reliable translational model to evoke mechanical rectal pain in rats and humans.

Methods: Mechanical rectal rapid balloon distension was done on two different days in 12 rats (separated by 24.3 ± 7.1 days) and 18 humans (separated by 9.3 ± 1.3 days). Evoked potentials were recorded from permanently implanted skull-electrodes in rats, at stimulation pressure of 80 mmHg and duration of 100 ms. In human surface electrodes and individualized pressure, corresponding to the pain detection threshold, lasting 150 ms, were used. Within- and between days reproducibility were assessed in terms of latencies, amplitudes and frequency content.

Results: In both rats and humans evoked potentials with tri-phasic morphology were recorded. No differences in latencies, amplitudes and power distribution were seen within or between days (all $F \leq 2.0$; all $P \geq 0.2$). The analyses of the EPs revealed peak-to-peak amplitude as the most reproducible parameter within (ICC ≥ 0.84) and between (ICC ≥ 0.70) days, seen across both species. The spectral analyses showed that the EEG power was distributed mainly in the delta and theta bands. The main power in rats was contained in the theta band (45%), whereas humans had the predominant power in the delta band (46%).

Conclusion: A unique visceral translational platform was established to reliably assess neurophysiologic response to rapid balloon distension in rats and humans. The model provides an approach to study basic and clinical pain as well as pharmacological intervention.

http://dx.doi.org/10.1016/j.sjpain.2012.05.036