amplitude of EPSPs and EPSCs. Brush or pinch stimulation was applied to the contrateral hindlimb.

Results. In normal rats, almost all SI neurons exhibited a bursting activity which had frequency of −0.9 Hz and amplitude of −90 pA. These burstings occasionally intiate a single or multispikes under the current clamp mode. In inflamed rats, the frequency was slowed and the duration of each bursting was prolonged. These burstings were completely inhibited by CNQX, indicating that the bursting activities are summation of glutamatergic inputs.

Conclusion. These findings together with our previous observations suggest that the inflammation causes the change in the synchronization of the outputs from the thalamus to SI neurons.

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LACOSAMIDE, AN INVESTIGATIONAL ANALGESIC, DOES NOT SHOW POTENTIAL FOR ABUSE LIABILITY OR DEPENDENCE IN PRECLINICAL TESTS

N. Krebsfaenger *, T. Stoehr

Department of Pharmacology and Toxicology, Schwarz Biosciences GmbH, Monheim, Germany

Lacosamide is an investigational analgesic that is currently being evaluated in phase III clinical trials for painful diabetic neuropathy. It has a novel, dual mode of action: selective enhancement of sodium channel slow inactivation and modulation of CRMP-2. Since lacosamide acts in the central nervous system via a novel mechanism of action, it was assessed in a number of targeted preclinical studies in line with the EMEA ''Guideline on the non-clinical investigation of the dependence potential of medicinal products''.

No binding within the therapeutic concentration range was detected in radioligand binding experiments with lacosamide and its major human metabolite for binding to 20 abuse- or dependence-related molecular targets.

When rats were trained to discriminate between lacosamide and saline in a 2-choice, lever-pressing, drug discrimination procedure, lacosamide did not evoke a robust subjective cue. Generalization testing revealed a lack of dose-related or consistent generalization to the lacosamide discriminative cue following administration of drugs with abuse potential from similar pharmacological classes (i.e. diazepam, phenobarbital, morphine and phencyclidine). Consistent with these findings lacosamide was not rewarding in a place-preference test or reinforcing in an i.v. self-administration procedure in rats.

After prolonged administration to rats and dogs, there was no tolerance to lacosamide's pharmacological actions and abrupt cessation of treatment did not produce psychological and/or physical dependence.

Overall, the preclinical assessment predicts that lacosamide will not have any potential for abuse liability or dependence in man. This is consistent with its mode of action which has not been associated with drug abuse or dependence.

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COLD SENSITIVITY IS INCREASED IN SPINAL DORSAL HORN WIDE DYNAMIC RANGE (WDR) NEURONS IN SPARED NERVE INJURY (SNI) RATS

L. Luo *[,a], H. Gustafsson [b], K. Hygge Blakeman [b], K. Angeby-Moller [b], O.-G. Berge [b]

[a] *Molecular Pharmacology, AstraZeneca R&D, Sodertalje, Sweden*

[b] *Disease Biology, AstraZeneca R&D, Sodertalje, Sweden*

Background and aims. In the SNI model of neuropathic pain, animals exhibit hypersensitivity to stimulation by cold spray (ethyl chloride). Here, we investigate the response properties of spinal dorsal horn WDR neurons to thermal stimuli following peripheral nerve injury in this model.

Methods. Under isoflurane anesthesia, 24 male Sprague–Dawley rats were subjected to tight ligation and transection of the left tibial and peroneal nerves. Following the nerve injury, rats developed mechano-cold hypersensitivity. Sixteen to 26 weeks later, single neuron recording was performed bilaterally on deep spinal dorsal horn WDR neurons. Sensitivity of the neurons to cooling of the skin from 32 to 4 °C, and heating from 32 to 50 °C was characterized.

Results. Respectively 64 and 68 mechanosensitive WDR neurons were recorded ipsi- and contralaterally to the injury. Spontaneous activity was significantly higher on the injured side (1.44 ± 0.61 spikes/s) compared with the contralateral side (0.08 ± 0.03 spikes/s; $p < 0.05$, mean ± SEM). A significant increase in the number of neurons responding to skin temeratures in the range of 4–17 °C was recorded on the injured side (33/64 U) compared with the contralateral side (14/68 U; $p < 0.001$). In contrast, no difference between sides was observed in the sensitivity to higher temperatures, in temperature thresholds, or in the number of spikes generated by any particular stimulus.

Conclusions. Following peripheral nerve injury, cold sensitivity was increased in dorsal horn neurons and/or