Effect of pre-emptive Vagus Nerve Stimulation on cortical spreading depression in rat
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Background There is some evidence from studies in refractory migraine and collateral effects
in epilepsy that vagus nerve stimulation (VNS) may be beneficial for migraine. This could be
due to anti-nociception in the trigeminovascular system or to an effect on cortical spreading
depression (CSD). While we have demonstrated the former in rats, there is up to now no study
of the latter.
Objective To determine the effect of VNS on KCl-induced CSD in rat using the implantable
devices employed in epileptic patients.
Methods We implanted stimulation electrodes around the left vagus nerve in the neck and the
stimulator (NCP-Cyberonics®) subcutaneously on the back of Sprague-Dawley rats. VNS
was applied for 5 days with a “classical” (30sec ON-5min OFF) or a “stringent” duty cycle
(21sec ON-18sec OFF). As controls, we used implanted, but non stimulated rats (ShamVNS)
and 28 day-treatment with valproate, a known CSD inhibitor. CSDs were elicited under
chloral hydrate anaesthesia by applying 1M KCl over the occipital cortex with a cotton ball.
The electrocorticogram was recorded ipsilaterally (DC-100 Hz) with parietal and frontal
electrodes for 2 hours.
Results Our preliminary data show that valproate decreases occurrence of CSD whereas both
VNS protocols have no effect.
Conclusion While this study confirms that chronic valproate treatment in rat reduces
susceptibility to CSD, it also shows that VNS has no significant effect on CSD, even when
delivered with a stringent duty cycle. A beneficial VNS effect in migraine is thus unlikely to
be CSD-mediated.