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.