

VNS in pain

The first investigations on the modulation of nociception by vagal afferents were performed approximately 20 years ago. Contrasted results emerged from experiments in animal with pro-nociceptive or anti-nociceptive actions of VNS depending on the stimulus parameters and the species examined. It appears that low intensity stimulations of cervical vagal afferents facilitate, but high intensity stimulations inhibit nociception. The analgesic effects of VNS seems to depend on a critical stimulation intensity that activates C fibres.

Recently, cervical vagal nerve stimulators have been implanted in humans for epilepsy treatment and pain studies have been conducted in such patients. Those clinical data confirmed the complexity of VNS effects with contradictory results reported on pain thresholds. Indeed, in one study, VNS induced a significant decrease of thermal thresholds when low intensity stimulations were used during the “ON” cycle (acute effects). In an other study, VNS induced on the contrary, an increase in mechanical pain thresholds independently of the ON-OFF cycles (chronic effects) but no changes of heat pain thresholds. However, beside clinical experimental studies, recent reports have described reductions in headache frequency and headache intensity 1 to 3 months after VNS treatment initiation in epileptic migraine sufferer patients and a pilot study showed a beneficial effect of VNS in chronic daily headache patients. Furthermore, thalamic activation demonstrated with positron emission tomography during VNS in epileptic patients as well as hypothalamic activation associated with increased release of ACTH and corticosterone could be some of the supraspinal mediators of antinociceptive and anti-inflammatory effects of VNS.

Prior to specifically applying VNS in the treatment of refractory pain in humans, the most efficient stimulation protocol need to be defined and underlying neuronal pain control processes in those conditions better understood. We have therefore used a commercially available device (NCP-Cyberonics) to examine the effect of left cervical VNS on several kinds of pain model in rat involving acute or inflammatory pain. We demonstrate clear antinociceptive effects under different VNS conditions including with parameters tolerable by patients, i.e. those already used in epilepsy therapy. We also show that several structures could be involved in those VNS analgesics effects among them the caudal trigeminal nucleus.

All together, those data suggest that VNS may be effective in the treatment of pain and potentially useful in resistant head and facial pain syndrome.