Available preventive drug treatments have only partial efficacy in primary headaches and most of them cause unpleasant side effects. Moreover, the chronic forms, the most disabling ones, become notoriously resistant to prophylactic pharmacotherapy. Alternative therapies have thus been developed. Nerve blocks, for instance, are used since a long term, but RCTs of their efficacy are scarce. Suboccipital infiltrations are the most useful. They consist of an injection in the vicinity of the greater occipital nerve of a steroid and a local anaesthetic. Various steroids have been used, but the best results seem to be obtained with mixtures of short- and long-acting compounds. In most studies, an injection of only a local anaesthetic has no, or a very transient, effect. In cluster headache (CH), for instance, several studies have shown that a suboccipital steroid-lidocaine infiltration is clearly superior to placebo, exceeding a 70% efficacy rate, both in the episodic and the chronic form of the disorder. Side effects are minor and transient, but focal alopecia, reported only with superficial injections, should be avoided by injecting into deep structures. Suboccipital infiltrations are also efficient in other trigeminal autonomic cephalalgias, hemicranias continua, fixed unilateral migraine, cervicogenic headache and occipital neuralgia. In refractory CH alcohol or steroid infiltrations of the sphenopalatine ganglion may also be useful, but the effect seems to be transient and there no placebo-controlled trials.

Various invasive central and peripheral neurostimulation procedures have been explored during the last decade in patients with refractory headaches. At least 1200 headache patients have implanted neurostimulation devices worldwide, but evidence-based data is scarce and many trials are still open or still ongoing. There is convincing evidence that deep brain stimulation of the ventro-posterior hypothalamus (hDBS), an area hyperactive during attacks in functional imaging studies, is effective in refractory chronic CH patients, but this is not a riskless procedure. Such patients should first undergo percutaneous occipital nerve stimulation (ONS). ONS has overall an efficacy similar to hDBS (>60% responders) but no serious side effects. Its mode of action is likely neuromodulation of the descending pain control system without any effect on the hypothalamic “generator” which explains why attacks most often recur when the stimulator stops functioning. ONS has also modest efficacy in chronic migraine, but more studies are needed. A recent sham-controlled trial has shown that (blocking) stimulation of the sphenopalatine ganglion with an implantable stimulator that can be activated on demand by an external remote controller is effective both for acute treatment and prevention of attacks: overall 68% of patients responded for either one or both.
Non-invasive neurostimulation methods are of major interest in headaches, as, thanks to their excellent tolerability, there use can be extended to less disabled patients with episodic headache. Transcutaneous supraorbital stimulation (SNS) was superior to placebo in a recent sham-controlled trial for the prevention of episodic migraine. The 50% responder rate of 38.1% is below that of topiramate (45%), but contrary to the latter that is abandoned by 1 patient out of 4 because of intolerance, SNS is quasi devoid of adverse effects. By contrast with peripheral nerve stimulation that module indirectly brain areas playing a role in headache pathophysiology, transcranial repetitive magnetic (rTMS) and direct current stimulations (tDCS) aim at influencing directly cortical and subcortical structures known to be abnormal in disorders like episodic and chronic migraine. It is known, however, from imaging and neurophysiological studies, that these abnormalities differ over the migraine cycle and between the two forms of migraine. While this has little relevance for peripheral nerve stimulation, it is of uttermost importance for transcutaneous neuromodulation where the target and the planned change in activity have to be clearly defined. We will illustrate this by comparing the negative results of studies using rTMS or tDCS to inhibit the visual cortex to prevent episodic migraine and preliminary results we have obtained recently with excitatory stimulation protocols in episodic migraine and inhibitory protocols in chronic migraine. Studies of novel devices targeting the vagus nerve with transcutaneous stimuli to treat acutely and prophylactically migraine and cluster headache are underway.

To summarize, so-called nerve blocks have added value in trigeminal autonomic cephalalgias and some other primary and secondary headaches. The future for neuromodulation, in particular the non-invasive methods, is bright as long as evidenced-based data support their efficiency and further research allows to understand how they act.

**Brief Biography**

Jean Schoenen, MD, PhD, after graduating from high school “Collège Patronné” in Eupen, has gained his medical degree in 1972 from Liège University. He was for 2 years an International Fogarty Fellow in the departments of Neurology and Neuropathology of the Massachusetts General Hospital-Harvard Medical School where he obtained certificates in Clinical Neurophysiology and Neuropathology. He is board-certified neurologist since 1979 and holds doctoral and post-doctoral degrees from Liège University. He was Research Director of the National Fund for Scientific Research-Belgium and Clinical Professor in Neurology before taking over Full Professorship at Liège University in 1998. He is acting chairman of the Department of Biomedical and Preclinical Sciences at the Faculty of Medicine – Ulg. His Research has focused on headache and spinal cord anatomy and pathology. He is leading the Headache & Neuronal Regeneration Research Unit and Headache Clinic at Liège University. He has 908 publications among which 398 peer-reviewed articles (H index: 56 after 1996), 92 book chapters and 4 books. He is Associate Editor of Cephalalgia and Editor-in-chief of Acta Neurologica Belgica. He is a former President of the International Headache Society and of the Belgian Neurological Society. He is founding past president of the Belgian Brain Council.