

Feasibility of simultaneous vagal nerve and deep brain stimulation in chronic cluster headache: case report and considerations

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Abstract In pathologies, such as refractory epilepsy, major depression and cluster headache, there could be indication to both vagal nerve stimulation (VNS) and deep brain stimulation (DBS). In particular, Mauskop (Cephalalgia 25:82–96, 2005) reported the efficacy and safety of VNS in chronic cluster headache. At our Institute, we perform posterior hypothalamic DBS for such clinical condition since 2000 and results appear to be encouraging. Here, we report the case of a patient with chronic cluster headache (CCH) who had initially improved after DBS, whose clinical effect subsequently diminished after head trauma; we performed VNS in the same patient, thus obtaining a new 50% reduction in frequency of pain bouts. Such benefit and the absence of any side effects (possibly due to the co-existence of the two systems) may suggest the possibility of a second therapeutical chance not only in CCH but also in the other two above-mentioned severely disabling pathological conditions.

Keywords Simultaneous stimulation ·
Vagal nerve stimulation · Deep brain stimulation ·
Cluster headache

Introduction

Indications to deep brain stimulation (DBS) can sometimes overlap the indications to vagal nerve stimulation (VNS) as

may happen in drug-resistant epilepsy [1, 2], major depression [4, 7, 10] and in chronic cluster headache patients [3, 6, 9]. So it may happen that patients harbouring deep brain electrodes could also be potential candidates to VNS or viceversa. The above-mentioned condition occurred in one patient affected by chronic cluster headache (CCH) who had been submitted at our Institute to ipsilateral hypothalamic DBS, which induced remission of pain bouts for 1 year. After such period, and after trivial head and neck trauma, pain bouts recurred and VNS implant was performed and activated simultaneously to the DBS system. The latter procedure led to a subsequent clear improvement of algic symptomatology.

This is the first report in literature referring to DBS and VNS systems working simultaneously in the same patient without side effects due to interferences between the two electrical systems.

Case report

A 60-year-old patient, 20 years ago, started to complain about intense right supraorbital and intraorbital pain attacks, which was initially episodic (about one episode per month), but rapidly assumed to a frequency of about eight per month. The pain attacks were accompanied by profuse tearing, conjunctival injection, eyelid swelling and nasal congestion. The clinical diagnosis of cluster headache was then formulated and patient initiated pharmacological daily treatment with verapamil, lithium, methysergide, valproate, topiramate, lamotrigine, pregabalin, gabapentin and other drugs including steroids in increasing dosages and several combinations, though without any clinical benefit. The only treatment which led to a partial and temporary amelioration of symptoms was sumatriptan,

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which the patient assumed at on-need basis at the onset of attacks.

Intensity and frequency of pain bouts anyway continued to increase with time despite such treatment; their duration ranged from 30 min to 4 h, and they presented over 200 times per month. After neurological and neurosurgical evaluations, in 2003, he then underwent DBS of right posterior hypothalamus [6] at our Institute.

The stimulation parameters were set at 2 V, contacts 0 and 1 as cathodes and case as anode, 30 Hz in frequency and 60 μ s as pulse width. The postoperative course was characterized by prompt and significant improvement of symptomatology with total remission of cluster headache attacks for 1 year. The surgical treatment allowed the patient to suspend the pharmacological treatment as a whole.

Unfortunately, after an accidental trauma of the head and neck occurred at 1 year after surgery, painful attacks gradually recurred, though not reaching the preoperative severity (duration of about 30 min, frequency of about 9 per day).

Radiological evaluation and pulse generator's check did confirm the structural integrity and functionality of the system and ruled out exhaustion of the battery of the pulse generator. The patient also underwent serial clinical evaluations with progressive increase of stimulation amplitude and several modification of the remaining stimulation parameters, again without substantial clinical benefit; the previous employed parameters were then reset.

Pharmacological treatment was resumed, but again the only beneficial drug was sumatriptan, assumed at the onset of attacks. So the patient assumed an average dosage of 60 mg sumatriptan in 24 h.

Taking into account the beneficial effect of VNS in CCH previously reported in the literature [9], we decided to perform implantation of VNS system to add peripheral neuromodulation to the still acting central modulation sustained by DBS.

Left VNS system implantation was performed in January 2008; the preoperative frequency and mean duration of pain attacks were about 270 per month and 30 min, respectively.

After VNS, the patient underwent regular clinical follow-up evaluations (every week for the first postoperative month and then on a monthly basis for 1 year in order to record both clinical changes and eventual side effects). The final VNS parameters (set at 1 month postoperatively) were: 0.75 mA, 30 Hz, 500 μ s, 30 s on stimulation and 5 min off stimulation.

The improvement of symptomatology began after 3 weeks from intervention and progressed gradually over time; at the last observation carried forward, the frequency of pain attacks was 120 per month and their mean duration

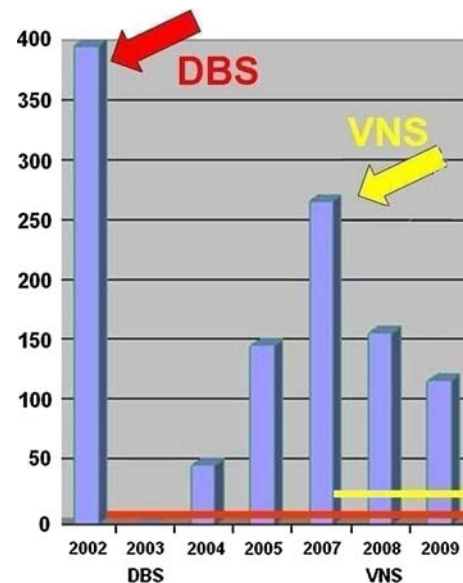


Fig. 1 Monthly frequencies of cluster headache pain bouts in our patient in function of time and presence of the two stimulating systems

was of 15 min with a reduction of 50% for both compared to pre-VNS period.

It is important to note that impedance testing of both stimulation systems were repeatedly performed at every postoperative visit, and their values did not change when the two systems were working together with respect to each of the two systems working alone (the other one being voluntarily switched off). Furthermore, no adjunctive stimulation-related side effects, potentially due to each of the two electrodes, were reported by the patient after the second intervention (VNS).

The course of frequency of pain attacks in this patient with respect to time is schematized in Fig. 1.

Discussion and conclusions

Emerging applications and recognized applications of VNS may overlap the field of DBS. This potential “double indication” may take place in the treatment of severe refractory diseases such as CCH [3, 6, 9], major depressive disorder [4, 7, 10] and unresectable refractory epilepsy [1, 2]. Patients harbouring DBS may take further advantage from VNS as happened in this reported case. Otherwise it is likely that patients not responding to VNS performed to treat depression or epilepsy could undergo DBS to treat the same disease.

Nevertheless, the interactions between peripheral neuromodulation (VNS) and central neuromodulation (DBS) are still poorly known and investigations in this field are needed. VNS has been reported to benefit CCH patients

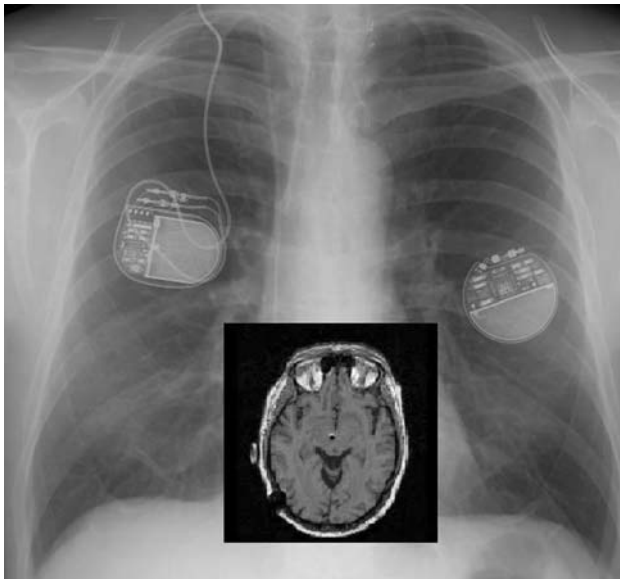


Fig. 2 Postoperative chest X-ray image of our patient showing the presence of the (*right* and *left*) infraclavicular pulse generators belonging to the two different stimulation systems; at the *left*, the VNS IPG; at the *right*, the DBS IPG. In the small *inset*, the patient's postoperative brain MR showing the location of the right hypothalamic DBS electrode

through peripheral mechanisms [2] different from the central mechanisms invoked to explain the therapeutic effects of posteromedial hypothalamic stimulation [3].

The reported case demonstrate that working VNS and DBS at therapeutic levels may cohabitate in the same patient without side effects provoked by the interactions of the two electrical fields (Fig. 2). In our opinion it may happen because VNS is a bipolar stimulation between two very close active contacts. DBS may also work in bipolar modality, but usually chronic stimulation is performed in unipolar configuration with case positive. A possible synergic effect could be suggested by the improvement observed in these patients after that VNS was added to DBS. Different monopolar and bipolar configuration have been tested during VNS and both resulted safe and without side effects.

The reason why, after occurrence of a trivial head and neck trauma cluster headache attacks recurred in spite of a still working DBS system (at the same parameters which had allowed a complete disappearance of symptomatology for 1 year) is not so clear; nevertheless, it is known that the course of the disease may suddenly change in response to environmental factors and traumatism [8, 11].

The altered balance between peripheral and central mechanisms which are considered in the physiopathology of the disease may also be responsible for the recurrence of pain bouts and a sort of tolerance to hypothalamic stimulation may be taken into account, as well as possible further worsening of the disease which could have become less responsive to DBS itself.

To explain the beneficial effect of VNS in this CCH patient we have to consider the central effects of peripheral neuromodulation which interacts with the same brainstem nuclei and circuits involved in CCH pathophysiology such as the raphe nuclei where central (DBS) and peripheral (VNS) signals may converge [5].

Anyway this case report remarks the emerging role of neuromodulation procedures in the treatment of extremely severe forms of trigeminal autonomic cephalalgias (TACs) when conservative treatments fail. The possible role of VNS originally proposed by Mauskop [9] has been confirmed and its feasibility in a patient harbouring DBS electrodes has been demonstrated.

To our knowledge, this is the first report of such a therapeutical combination in man and its value could go beyond cluster headache's treatment, stimulating the research in other fields such as major depressive disorder and refractory epilepsy, giving to these severely impaired patients a second therapeutical chance when the first choice treatment fails or loses its efficacy.

Conflict of interest statement The authors declare that they have no conflict of interest related to the publication of this manuscript.

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