Clinical Neurology and Neurosurgery 110 (2008) 755–762

Clinical Neurology and Neurosurgery

www.elsevier.com/locate/clineuro

Review

Vagal nerve stimulation: Exploring its efficacy and success for an improved prognosis and quality of life in cerebral palsy patients

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Received 4 November 2007; received in revised form 29 April 2008; accepted 9 May 2008

Abstract

Cerebral palsy (CP) continues to pose a cause for major socioeconomic concern and medical challenge worldwide. It is associated with a multi-faceted symptomatology warranting a multi-dimensional management-approach. Recent recognition of neurocognitive impairment and its hopefully possible treatment has opened up a new dimension in its management to the neurologists. Vagal nerve stimulation (VNS) technique is presently emerging as an effective alternative anti-epileptic therapeutic measure in intractable epilepsy. VNS has recently been shown to possess a suppressive effect also on interictal epileptiform discharges (IEDs) that are now being widely accepted as established associates of neurocognitive impairment. In this paper, the author proposes VNS technique implantation in CP patients on account of its dual therapeutic effectiveness, i.e. anti-epileptic and IED-suppression. These two effects are likely to control seizures that are quite often drug-resistant and also improve neurocognition in CP patients, thus hoping for a better overall prognostic outcome and an improved quality of life of the CP patients by VNS.

Keywords: Cerebral palsy; Neurocognitive impairment; VNS; Interictal epileptiform discharges; Quality of life; Epilepsy

Contents

1. Introduction

Cerebral palsy (CP) is essentially a motor disorder due to non-progressive brain damage and commonly associated with epilepsy (that is frequently drug-resistant) and significant neurocognitive impairment, hence warranting a multi-dimensional approach to its management. Since the disorder continues to assume a global major socioeconomic

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doi:10.1016/j.clineuro.2008.05.005

concern, newer and improved therapeutic interventions also continue to come into light.

This paper is intended to explore possibility of a beneficial role of vagal nerve stimulation (VNS) technique in a hope for a better prognostic outcome and an improved quality of life (QOL) in CP management of especially small children presenting with intractable seizures, as the purpose of VNS application is to attain an early suppression of the seizures and interictal epileptiform discharges (IEDs) keeping in view that improvement in cognitive functioning is more likely when an early intervention to suppress seizures and/or IEDs is instituted.

CP is commonly associated with mental retardation and seizures [1,2]; further, proportion of intractable seizures (medically refractory) has been reported to be high in CP [2] and mentally retarded children [3]. Incidence of epilepsy in CP ranges from 30 to 60% on account of diverse variations in its manifestation. Spastic forms of CP are more frequently associated with epilepsy. EEG abnormalities have been detected in more than 90% of epileptic CP patients in one study [4]. It has been found that pediatric population shows better and more rapid response to VNS-mediated decrease in IEDs and electrographic seizures that leads to early onset of sense of well-being and improved QOL [5]. Therefore, VNS in such cases can be of high therapeutic value by virtue of its anti-epileptic as well as IED-suppressive effects.

2. Neurophysiology of interictal epileptiform discharges

Interictal epileptiform discharges represented by spike, spike-wave and sharp wave have for long been regarded as reliable indicators of epileptogenic regions [6–9]. For more than 50 years, IEDs recorded by scalp EEG have been viewed as hallmark for diagnosing and classifying the type of epilepsy [10]. Some researchers consider interictal scalp IEDs as more reliable indicators of epileptogenic foci than ictal discharges [11] because of the latter spreading all over the brain and also being associated with movement artifacts, which can obscure the IEDs. Present studies have however demonstrated that IEDs are also commonly associated with neuropsychological disturbances other than epileptic disorders.

Epileptogenic regions defined by MRI/PET/SPECT studies and/or favorable post-surgical outcome have helped in clearly identifying the source of IEDs in the majority of epilepsy patients. IEDs have also been found to correlate well with functional MRI (fMRI) activation areas [10]; in addition, fMRI studies have also detected association of local changes in blood oxygenation with IEDs [10]. Involvement of a cortical area of at least 10 cm^2 has been found to be necessary for recording well-identifiable scalp IEDs [11]. “Irritative” and “epileptogenic” zones of cerebral cortex although may not be identical do share a close spatial relationship and IEDs are presumed to be generated from the “irritative” zone.

For detection of interictal epileptiform discharges, it is recommended that a sleep-EEG be performed to ensure maximum chances of yielding IEDs. Detection of IEDs can be enhanced by magnetoencephalography (MEG). Knutsson et al. have shown that interictal biomagnetic signals are more precise locators of epileptic activity in patients with intractable seizures [12]. Pataraia et al. [13] report that a simultaneous EEG and MEG study can provide comprehensive information on functional organization of spikes, the study being done on patients of benign rolandic epilepsy of childhood. Shibasaki et al. suggest that MEG can be used not only to identify the epileptic focus but also to investigate the functions of cortical areas at or near the epileptic focus or the structural lesion [14]. RamachandranNair et al. have shown in patients with intractable epilesy that MEG is a reliable predictor of surgery-outcome when MRI findings are normal or non-focal [15].

3. Role of EEG synchronization and de-synchronization in neurophysiology of spikes and epileptogenesis

It is now well accepted that EEG synchronization forms the main underlying basis for epileptogenesis whereas de-synchronization exerts resistance to it and therefore acts as an anti-epileptic state. It is believed that epileptic seizures occur due to hypersynchronous discharges [16]. Spiky epileptic discharge is an indicator of greater synchronization of unit cell populations [17] seemingly caused by synchronization of population group 1 neurons [18].

Anterior thalamic stimulation (low frequency) is found to lead to cortical synchronization and increased susceptibility to epilepsy, whereas high-frequency stimulation leads to de-synchronization and resistance to epileptic attacks [19]. Neural generators of synchronous EEG oscillations during non-rapid eye movement (NREM) sleep can promote electrographic seizure propagation whereas those of asynchronous neuronal discharge reduce electrographic seizures during rapid eye movement (REM) sleep and wake alert state [20]. Hypersynchrony induced by NREM sleep facilitates both initiation and propagation of partial seizures [21], hyperventilation also induces synchrony and can precipitate epileptic attacks [22]; therefore, NREM sleep and hyperventilation are both used as provocative techniques during EEG recording especially in suspected epileptic patients. REM sleep on the other hand, characterized by low voltage fast activity (de-synchronization) is known to be associated with marked reduction, at times total absence of seizures, generalized bursts and abnormal discharges in EEG [21–23]. Some neuroscientists consider REM sleep as the most anti-epileptic state in human wake-sleep cycle [24]. Similarly, wake alert state, which also is associated with EEG de-synchronization is known to reduce seizure frequency [18].

IEDs cannot be viewed as benign or randomly occurring events. They do posses a definite pathophysiology underly-