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Review

Changes in sleep patterns after vagus nerve stimulation, deep brain stimulation or epilepsy surgery: Systematic review of the literature

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A B S T R A C T

Purpose: Perform a systematic review of the literature on the effects of vagus nerve stimulation (VNS), deep brain stimulation (DBS) and epilepsy surgery in subjective and objective sleep parameters.
Methods: We performed a literature search in the main medical databases: Medline, Embase, Cochrane, DARE and LILACS, looking for studies that evaluated the effects of VNS, DBS or epilepsy surgery on sleep parameters. In all, 36 studies, coming from 11 countries, including reviews, cohort studies, case series and case reports were included.
Results: VNS induces sleep apnoea dependent of the stimulation variables. This condition can be reverted modifying these settings. Surgical procedures for epilepsy cause an improvement in objective and subjective sleep parameters that depend on the success of the procedure evaluated through ictal frequency control. There is evidence that non-pharmacologic treatment of epilepsy has different effects on sleep patterns.
Conclusion: It is advisable to include objective and subjective sleep parameters in the initial evaluation and follow-up of patients considered for invasive procedures for epilepsy control, especially with VNS due to the risk of sleep apnoea. More high quality studies are needed.

1. Introduction

In patients with epilepsy, multiple factors such as ictal frequency, interictal activity and anticonvulsant therapy affect sleep architecture and quality [1]. Daytime somnolenceis the most common complaint of patients with epilepsy is [1,2]. An increase in obstructive sleep apnoea/hypopnea syndrome (OSAHS) has been documented in patients with refractory epilepsy, in whom, with an incidence as high as 33% [3], associated with a decline in the quality of life [4].

The objective of this systematic review was to evaluate current evidence on the effects of non-pharmacological treatments, including vagal nerve stimulation (VNS), deep brain stimulation (DBS) or epilepsy surgery on both objective and subjective sleep parameters.

2. Methods

2.1. Search strategy

We performed a systematic review of Medline (Pubmed), Embase, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects – DARE and Latin American and Caribbean Literature in Health Sciences – LILACS. Terms used and adapted for each database were:

(epilepsy OR epilepsies OR epileptic OR seizures)
AND
(surgery OR surgical OR "deep brain stimulation" OR DBS OR callosotomy OR lobectomy OR vagus)
AND
(Sleep OR REM OR insomnia OR somnolence OR sleepiness OR polysomnography OR somnography OR hypersomnia OR parasomnia OR osa OR apnea OR dreams)

We limited the search to articles with abstract available and published from January 1, 2000 to the present (search date June 15, 2016). There was no language restriction. We included meta-analyses or systematic reviews, randomized clinical trials, cohort studies, case series or individual case reports, focusing on the effect

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of epilepsy surgery, VNS or DBS on objective or subjective sleep parameters.

Initial exclusion of irrelevant articles, based on title and abstract, was done by 2 independent members of the research group (ORO, SGT); full-text versions were obtained for data extraction. The list of references of each study was analysed manually. Subsequently, the articles were classified according to the type of procedure, and according to the American Academy of Neurology's classification of evidence [5].

3. Results

Fig. 1 shows the selection process. The initial search retrieved 2717 references, of which finally 36 articles with a class of evidence III and IV were reviewed; 15 came from United States; five from Italy, four from France; three from Canada, two from Sweden, and one each from Australia, Austria, Brazil, Cyprus, Finland, Germany, and India; 27 articles referred to VNS, 8 to epilepsy surgery and 1 to DBS.

3.1. Vagus nerve stimulation

Of the 27 articles on VNS (Table 1), 11 were case reports, nine prospective descriptive studies and seven retrospective descriptive studies. These included a total of 209 patients between the ages of 3 and 58 years.

The effect of VNS on subjective parameters of sleep quantified by daytime sleepiness was evaluated in three studies. Rizzo et al. [6], using a sleep diary, described an improvement of daytime sleepiness with the chronic use of the stimulator. The study by Malow et al. [7] found that the score on the Epworth scale improved from 7.2 ± 4.4 to 5.6 ± 4.5, unrelated to a decrease in ictal frequency or changes in the sleep stages through polysomnographic evaluation. These findings contrast with the case report of St Louis et al. [8] in which a patient developed snoring and an increase in the score on the Epworth scale following implantation of the VNS, both of which improved after reducing its pacing times.

Carrosela et al. [9] reported the case of a patient with deep sleep status epilepticus in which there was an improvement in the perception of well-being, also finding an association between the

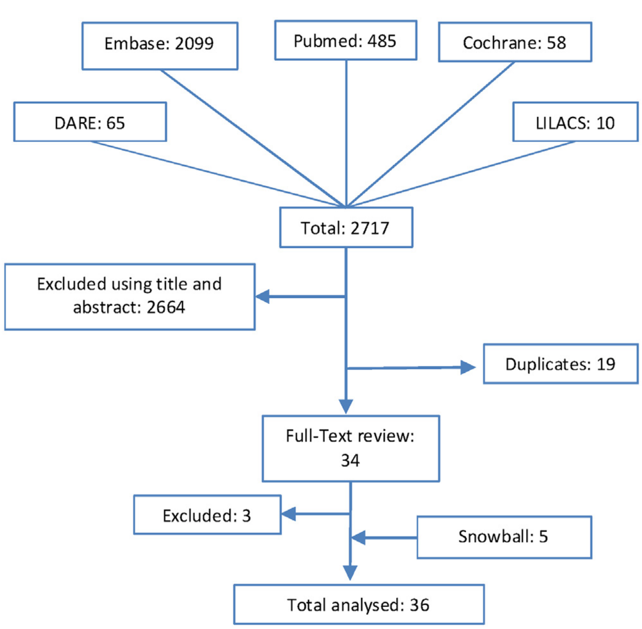

Fig. 1. Study selection process.

decrease in the number of crises with improvement in cognition, language, school performance and decrease in irritability. In the study by Galli et al. [10], quality of life was evaluated, finding an improvement related to decreased sleep latency as measured by the Multiple Sleep Latency Test (MSLT).

Objective evaluation using polysomnography showed a relationship between sleep disturbances and VNS in 16 studies [3,8,11–24]. During the ON period [9,14,19], the discharge frequency and the configuration with fast cycling (ON/OFF) [13,18] were associated with an increase in the apnoea-hypopnoea index (AHI), the number of awakenings [14], and a decrease in respiratory effort and tidal without alteration in the AHI [3,15,20]. In all cases, the occurrence of apnoea was correlated with the ON period of the stimulator, and turning it off, or adjusting the setting with decreased stimulation parameters achieved an adequate control of respiratory symptoms in most patients [8,11,17], others required positive pressure ventilation [15,22].

Two studies with polysomnographic evaluation described the presence of vocal cord adduction during the ON stimulation period, evidenced by indirect laryngoscopy, associated with the onset or worsening of respiratory sleep disorder [23,25], suggesting a possible explanation for the mechanism by which the stimulator induces sleep apnoea.

In children, disturbances in the cardiorespiratory regulation were described during stimulation activation, including an increase in frequency and a decrease in respiratory amplitude, with variable changes from patient to patient in heart rate, which results in poor optimization of tissue oxygenation [21,26]. In adults, tachypnoea was the only disturbance reported after the ON period, with no significant changes in heart rate [27].

Other reported polysomnographic findings associated with VNS are: higher intensity of the stimulator attenuates the REM sleep, whereas lower intensity improves the wakeful state [27]. Stimulator discharges are associated with a significant increase in respiratory rate and a decrease in the range of abdominal distension, inducing a decrease in oxygen saturation [28]. Finally, VNS induces a significant increase in slow-wave sleep and decreases both sleep latency and stage 1 [29].

The objective evaluation by means of electroencephalographic parameters (EEG) found that VNS produced an increase of the spectral power in the delta and theta wave EEG in non-REM sleep, and alpha waves in REM sleep and wakefulness, without significant decrease in interictal activity during sleep [30]. In the epileptic state of deep sleep, there was no epileptiform activity at the follow-up year, associated with cognitive improvement [9]. A decrease in the number of interictal epileptiform discharges, especially during REM and delta sleep were also described,as well as other minor alterations in the EEG [27].

3.2. Epilepsy surgery

Eight articles refer to the effect of epilepsy surgery on sleep [32–39] (Table 2); two of these are case-control studies, two prospective case series, two retrospective, and two case reports, with a total of 207 patients aged between 3 and 62 years.

In the class III study performed by Zanzmera et al. [32], 17 patients with refractory focal epilepsy, mostly of the mesial temporal type, followed by frontal and parietal, found a statistically significant reduction in ictal frequency ($p = .01$) with improvement in self-reported sleep parameters, such as the duration of night-time sleep ($p = .01$), total sleep duration ($p = .03$), and a reduction in Epworth score ($p = .02$) in patients with good postoperative outcome. In the polysomnographic study, a decrease in AHI was found in patients with good postoperative outcome with respect to the basal state and the poor outcome group.