Review Article
Pressure pain assessment may predict the outcome of spinal cord stimulation for refractory epilepsy

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Abstract: It was well-documented that epilepsy and pain arise from an excitation-inhibition imbalance within neuronal networks. A previous meta-analysis of data from clinical trials showed an association between anticonvulsants and specific pain types, e.g. multiple sclerosis pain. Multiple multicentre randomized controlled trials have shown that antiepileptic drugs have a prominent role in the treatment of several types of pain, e.g. neuropathic pain. Many anticonvulsants have been introduced to better manage acute postoperative pain, with improvements in analgesic efficacy and safety. These data suggested that there existed the similar mechanisms of certain forms of epilepsy and pain, and the therapeutic mechanism of spinal cord stimulation for certain forms of epilepsy and pain may be involved in the melanocortinergic signaling, and the change in cerebral glucose metabolism. We hypothesized that pressure pain assessment may predict the outcome of spinal cord stimulation in refractory epilepsy.

Keywords: Pressure pain assessment, spinal cord stimulation, refractory epilepsy

Introduction

Spinal cord stimulation (SCS), also known as dorsal column stimulation, is a viable alternative treatment modal for certain forms of drug resistant epilepsies [1-3]. Currently, however, the success of spinal cord stimulation cannot be preoperatively predicted. It was reported that an anticonvulsant drug gabapentin reduced postoperative pain and the need for opioids, and enabled earlier ambulation of the patient [4-6]. Data from clinical trials showed that pressure pain assessment predicted postoperative pain [7-10]. Nevertheless, it was still unclear whether pressure pain assessment predicted the efficacy of spinal cord stimulation in refractory epilepsy. We would like to further discuss this idea by introducing an electronic pressure algometer [10].

A previous meta-analysis of data from clinical trials showed an association between anticonvulsants and specific pain types, e.g. multiple sclerosis pain [11]. Multiple multicentre randomized controlled trials have shown that antiepileptic drugs have a prominent role in the treatment of several types of pain, e.g. neuropathic pain [12-17]. In addition, anticonvulsants, e.g. Gabapentin and pregabalin, have been introduced to better manage acute postoperative pain, with improvements in analgesic efficacy and safety [6, 18]. These data suggested that there existed the similar mechanisms of certain forms of epilepsy and pain.
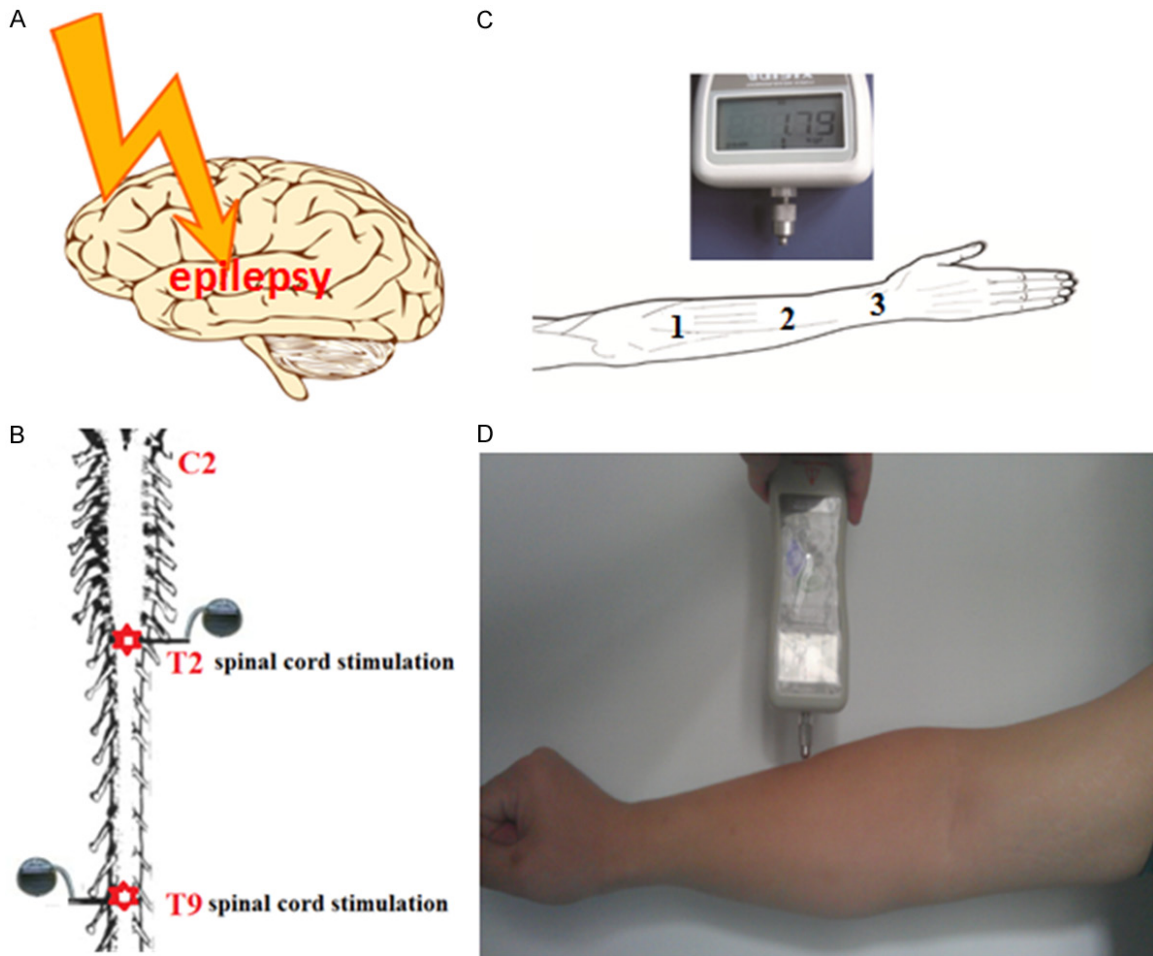
The hypothesis

It was well-documented that epilepsy and pain arise from an excitation-inhibition imbalance within neuronal networks [19-29]. As spinal cord stimulation (SCS) exists the some advantages of reversibility and adjustability, it is expected to have therapeutic effects for patients with intractable epilepsy. We hypothesized that pressure pain assessment may predict the outcome of spinal cord stimulation in refractory epilepsy.

Evaluation of the hypothesis

Recent work suggests that pressure pain assessment may predict postoperative pain

Figure 1. Schematic diagram of pressure pain assessment predicting the outcome of spinal cord stimulation in refractory epilepsy. A. Image of epilepsy attack. Epilepsy is a diverse neurological disorder in which excessive disruption to the brains activity causes recurring seizures or brief episodes of altered consciousness. B. Diagrams of cross sections of the spinal cord at cervical (C) and thoracic (T) levels. Anatomical plates taken from Brichta A.M. and Grant G. (1985) [31]. A small wire (called a lead) connected to a power source is surgically implanted under the skin. C. Mechanical algometer with a 0.1 cm^2 size probe. Locations 1, 2, and 3 on the right forearm. Some drawings were taken from Y. Duan (2013) [8]. D. Photograph showing how a digital algometer was used to apply stimulation to muscle on the right forearm.

[7-10]. There were three types of pain stimuli to be applied for the assessment of pain sensitivity: thermal, pressure, and electrical pain [7, 30-34]. Pressure stimuli, the most common stimulus applied to evaluate pain sensitivity, were delivered by use of a special stimulation device, e.g., the mechanical algometer [35, 36], a handheld pressure applier and a series of calibrated rigid filaments (von Frey hairs). These instruments provided a precise force over the skin (i.e., point pressure) for pressure pain analysis [37], despite the variable skin resistance. The pressure stimulation was usually applied over the forearm, the lower leg, ear, and fingers.

We introduced pressure pain assessment on muscle by an electronic pressure algometer. First, intensities were adjusted to cause weak and strong pain sensation (i.e., the pressure pain threshold and pressure pain tolerance) at a target site (i.e., the forearm) in preliminary testing. Next, perpendicularly applying around 1 cm^2 solid tip of an algometer probe (YISIDA-DS2, Hong Kong, China) on the surface (skin) at the lateral brachioradialis of the right elbow joint (**Figure 1**), the experimenter gradually increased the pressure at a speed of 1 kg/s until the subject verbally indicated that the stimulation was painful. At that point, when pain became intolerable, these values were

recorded. This procedure was repeated 5 min later, and the average of the three measurements was calculated. Duan et al. reported the profiles of pressure pain threshold (PPT) and pressure pain tolerance (PTO) of healthy undergraduates, and the results showed that the ranges reference ranges (kg/cm^2) of PPT were 1.19-4.63 in the males and 0.37-3.63 in the females [38]. This survey established the normal reference ranges of tenderness thresholds at the specific measuring spot for some specific population. These ranges may serve as a reference for the sensitivity of individual tenderness safely, accurately and simply [38].

Rapid advancements in neurostimulation technologies are providing relief to an unprecedented number of patients affected by debilitating refractory epilepsy [23, 39-41]. Preliminary reports demonstrated that high-frequency stimulation for anterior nucleus thalamus (ANT-HFS) is an effective treatment for patients who suffer from y epilepsy, and Yan [42] hypothesized that outcome of EA at acupoints could predict the therapeutic effect of ANT-HFS. Tian indicated that the mechanism of electroacupuncture for predicting the efficacy of stimulation targeted at subthalamic nucleus in epilepsy might be involved in the melanocortinergic signal [21, 43], and the change in cerebral glucose metabolism generated by electroacupuncture might predict the outcome of ANT stimulation in refractory epilepsy [21]. We think that the therapeutic mechanism of spinal cord stimulation for certain forms of epilepsy and pain may be involved in the melanocortinergic signaling, and the change in cerebral glucose metabolism.

Several lines of evidence have highlighted that the link between spinal cord stimulation and specific pain types is well established on many levels [44-50]. Some literature findings suggested a possible direct effect of spinal cord stimulation on the activating structures of brainstem motor regions, leading to increase the cortical and thalamic input [51]. Because the therapeutic mechanisms of spinal cord stimulation for certain forms of epilepsy and pain were similar [1, 2, 52, 53], we might predict better prognosis of spinal cord stimulation for patients with refractory epilepsy by reference to the pressure pain responses (including pressure pain threshold and pressure pain tolerance). There is only limited scientific evidence

to support the idea that pressure pain assessment may predict the outcome of spinal cord stimulation in refractory epilepsy. Further studies are warranted in this area.

Conclusion

Based on the above analyses, we propose a hypothesis that pressure pain assessment may predict the outcome of spinal cord stimulation in refractory epilepsy.

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Disclosure of conflict of interest

None.

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