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Research paper

Time-frequency patterns of somatosensory evoked potentials in predicting the location of spinal cord injury

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HIGHLIGHTS

- A high resolution time-frequency analysis (TFA) was applied to somatosensory evoked potentials (SEP).
- The pattern of SEP TFA is associated with the location of spinal cord injury (SCI).
- TFA of SEP after acute and chronic SCI at the same level presented a common distribution pattern.
- These common areas in TFA possess information about the site of neurological deficit.

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ABSTRACT

Somatosensory evoked potentials (SEPs) were found to exhibit different time-frequency patterns after acute spinal cord injury (SCI) at different levels, which implies that changes of these patterns may be associated with the location of SCI. Based on this finding, we propose the hypothesis that there are information regarding the location of SCI contained in the time-frequency patterns of SEPs. Purpose of the present study is to verify this hypothesis by comparing the time-frequency patterns of SEPs after acute and chronic SCI at the same level. The study examined the distribution patterns of the time-frequency components (TFCs) of SEPs before and after acute and chronic injury at C5 level in the spinal cord. Experimental results of SEP recordings from 24 adult rats show that there are common areas in the time-frequency distributions of SEPs. The TFCs from both the acute injury group and the chronic injury group are located in these areas with no TFCs from the normal group. Findings suggest that these areas are likely to possess information concerning the site of neurological deficits in spinal cord while independent of the modality of injury. This study provides basis for identification of stable time-frequency patterns of SEPs after different types and locations of SCI, which will guide the development of SEP-based SCI location detection.

1. Introduction

The conventional clinical method in diagnosing and localizing the neurological deficits after the spinal cord injury (SCI) is based on imaging, such as CT and MRI. It allows the abnormal morphology of the spinal cord compression to be shown. However, abnormal anatomy can often be found without any impairment to the neurological function [2,6,7,12]. Additionally, in cases of multiple level abnormalities, this method is difficult to ascertain the offending level.

In a recent research [13], it was found that changes of the time-frequency pattern of somatosensory evoked potentials (SEPs) are likely to be associated with the site of neurological deficits within the spinal cord. This means that the SEP time-frequency distribution (TFD) may contain information regarding the level of SCI. However, this research only analyzed the SEP TFD changes after acute injury to the spinal cord and therefore prompts the question that whether the same phenomenon can also be found in the SEP TFD after chronic SCI. If the answer is affirmative, it can confirm that the post-SCI SEP TFD does contain location information. If not, the changes of SEP time-frequency patterns may only be the pathological effects of the acute SCI. Therefore, this study is conducted for the evidence of locational information regarding the time-frequency pattern of SEP to be comfirmed in both acute and chronic SCI.

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2. Methods

2.1. Materials

A total of twenty four adult Sprague-Dawley rats weighting from 250 g to 300 g were used. They are divided into 3 groups, i.e. 1 normal group and 2 experimental groups, each contianing 8 rats. Both the acute and chronic injuries are induced at the C5 level in the spinal cord of the rats in the 2 experimental groups respectively.

2.2. Experimental procedure

2.2.1. Acute injury

During the experiments of acute injury, each rat is placed in a stereotaxic frame to keep its head stable and anesthetized with isoflurane (2% for induction and 1.5% for maintenance). The NYU-MASCIS contusion SCI model that has been widely used clinically for experimental SCI therapeutic and mechanistic research [14] is applied as the acute injury model. A 10-g rod at the height of 25 mm is dropped onto the exposed dorsal surface of the C5 level spinal cord to produce the acute SCI.

2.2.2. Chronic injury

The operations of producing chronic compression are performed under microscopy by a trained spine surgeon based on an established surgical protocol for implantation of water-absorbing materials [9]. The animals are operated under general anesthesia with 10% chloral hydrate intraperitoneally. After laminotomy, a water-absorbing polymer is inserted into the upper side of rat spinal canal at C5 level to deliver chronic compression to the spinal cord.

2.3. Data collection

For the acute injury group, SEPs are collected from the rats before and 60 ± 2 min (stationary phase) after weight drop contusion. For the chronic injury group, SEPs are recorded before and 3 weeks after implantation surgery. During SEP recording, isoflurane (1.5%) is used to maintain anesthesia. Cortical responses are evoked using a constant stimulator that generates a 4.1 Hz square wave 0.1 ms in duration to stimulate the median nerve along forelimb of the rats. The stimulation intensity is increased gradually until a mild twitch of the forelimb is observed.

All cortical SEPs are recorded over the forelimb area of the sensory cortex at a sampling rate of 10 kHz. The recorded signals are amplified 2000 times and isolated to 20–2000 Hz. The sweep time of SEP recording is 50 ms. A total of 200 SEP responses are averaged for each trial to achieve a good signal quality. All the recordings follow this procedure to ensure reproducibility. Data collection procedures are performed by SEP recording instrument (YRKJ-A2004, Zhuhai yiruikeji Co., Ltd., China).

2.4. Time-frequency analysis

Previous studies show that Matching Pursuit (MP) algorithm can be applied to the SEP signal to perform high resolution time-frequency analysis, by which the SEPs can be decomposed into a set of elementary waves (TFCs) [16,15]. In this study, the MP algorithm is adopted to the averaged cortical SEPs in order to calculate their time-frequency distributions and extract the TFCs within them.

The extracted TFCs with the highest relative energy (the power of the component divided by the power of the whole SEP signal) are defined as the 'main TFCs' in this study. In the experiment, the relative energies of all the main TFCs of the SEP signals in each group are above 0.3. TFCs with relative energy lower than 0.3 are defined as 'sub-TFCs' in this study.

Next, the peak time (latency), peak frequency of the main TFC in each TFD are measured and compared among groups. The mean value and standard deviation of the peak time and peak frequency in each group are caculated from all experimental rats.

Furthermore, the kernel density estimation algorithm are applied to the sub-TFCs in each group to estimate their joint probability density function (PDF) using Gaussian kernels [15]. Distribution areas of the sub-TFCs in different groups are outlined by their PDFs, respectively. Common regions can not only be distinguished between pathological and normal distributions, but also between acute and chronic distributions.

3. Results

SEPs from three rats are shown as representative waveforms in the normal, acute injury and chronic injury groups (first row, Fig. 1). The P1 and N1 parameters seen in the normal SEP waveform are present with differing latencies and amplitudes after acute and chronic injury.

TFDs of these waveforms based on MP algorithm are demonstrated in the second row in Fig. 1. The locations of the TFCs extracted by the MP algorithm can be found in these TFDs. The acute and chronic injury group have some common TFCs with similar distribution locations in time-freqency domain by visual inspection.

Next, the distribution patterns of the main TFCs are compared among the three groups. The locations of the main TFCs of the normal group SEP waveforms are within the region of 10–20 ms and 40–70 Hz (Fig. 2 (a)). The time and frequency (mean ± standard deviation) of them are 12.8 ± 2.5 ms and 54.9 ± 4.3 Hz, respectively. After acute injury, the main TFCs tend to have longer latencies (15.3 ± 2.9 ms) and a wider distribution range in the frequency domain (51.8 ± 11.8 Hz), as shown in Fig. 2 (a). However, these main TFCs of the acute injury group share a similar distribution area with the normal group. By contrast, the main TFCs of the chronic injury group have a distinct distribution pattern (Fig. 2 (a)). It can be observed in Fig. 2 (a) that the main TFCs of SEPs after chronic injury are mainly distributed from 20 to 40 ms in time domain and from 20 to 60 Hz in freqeuncy domain with one outlier, which is distinguished from the normal and acute injury group. The time and frequency of these TFCs are 26.6 ± 8.0 ms and 42.1 ± 9.7 Hz, respecively. The statistical comparison results show that the main TFCs of SEP after chronic injury have significantly longer latency and lower frequency compared with the normal and acute injury group (Fig. 2 (b, c)).

Apart from the main TFCs, distribution patterns of the sub-TFCs are also analyzed in Fig. 3. Positions and PDFs of the sub-TFCs are plotted in Fig. 3 (a–c) using distinct colors. It is worthwhile to note that TFCs from 0 to 5 ms are susceptible to the stimulation artifacts. Therefore they are excluded from the study. In Fig. 3 (a), the normal group sub-TFCs have a relatively compact distribution compared with the injury groups. In the time-frequency region between 5 and 20 ms and 20 to roughly 140 Hz, there are no sub-TFCs from the normal group. In the temporal range 35–50 ms, only one normal group sub-TFC is found. On the other hand, the acute and chronic injury groups have more diffused distributions as shown in Fig. 3 (b and c).

Additionally, there are peak areas of the joint PDF, where TFCs concentrate and have similar temporal and frequency features. In the PDFs, all the local peaks are detected. By checking the PDF values of all these peaks, we found that most local peaks have values lower than 20% of the maximum PDF value, and only two peaks in each group have relatively large PDF values (higher than 80% of maximum PDF value). These large PDF peaks are indicated by crosses in Fig. 3 and they are labeled as 'P1' and 'P2'. The two PDF peaks of the acute injury group have longer latency and lower frequency