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Charactering neural spiking activity evoked by acupuncture through state-space model

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ABSTRACT

In this paper, the underlying action mechanisms of acupuncture during neural spiking activities are studied. First, taking healthy rates as the experimental subjects, different frequencies of acupuncture stimulate their Zusanli points to obtain the evoked electrical signals of spinal dorsal horn neurons. Second, the spikes of the individual wide dynamic range (WDR) neuron are singled out according to wavelet features of different discharge waveforms and transformed into point process spike trains. Then we introduce a state-space model to describe neural spiking activities, in which acupuncture stimuli are the implicit state variables and spike trains induced by acupuncture are the observation variables. Here the implicit state process modulates neural spiking activities when driven by acupuncture. The implicit state and unknown model parameters can be estimated by the expectation–maximization (EM) algorithm. After that, model goodness of fit to spike data is assessed by Kolmogorov–Smirnov (K–S) test. Results show that acupuncture spike trains for different frequencies can be described accurately. Furthermore, the implicit state process involving the information of acupuncture time makes the potential action mechanisms of acupuncture clearer.

1. Introduction

Acupuncture is a typical treatment of disease in China and it puts the thin needles stab into the patient's skin at specific points to alleviate pain [1–3]. This has been supported by the current scientific researches [4–7]. Studies show that acupuncture can regulate the electrical activities of peripheral nerves, neurotransmitters and neurotrophic factors [8–12] and has underlying molecular effect mechanisms [13,14]. Cerebral blood flow, arterial blood pressure and heart rate are differentially modulated by different amplitudes and frequencies of acupuncture in human subjects [15]. But the reason why different acupuncture stimuli have different effects has not been found and the action mechanism of acupuncture is also not known.

Zusanli point is used more often in Acumox Therapeutics [16,17], which is located at the edge of tibias, beneath the knee (see Fig. 1). The induced spike trains of spinal dorsal horn neurons are enough to investigate the function mechanisms of acupuncture, because that acupuncture at Zusanli regulates activities of viscera just by spinal reflexes [5]. The acupuncture afferent pathways and central sites have been identified in the anterolateral tract in the spinal cord [18,19]. Acupuncture is noxious mechanical stimulation. Acupuncture stimulates Zusanli point as shown in Fig. 1 [20], and the action potential is generated at one branch of a peptide-containing C fiber through tissue damage and the release of chemical signaling factors,

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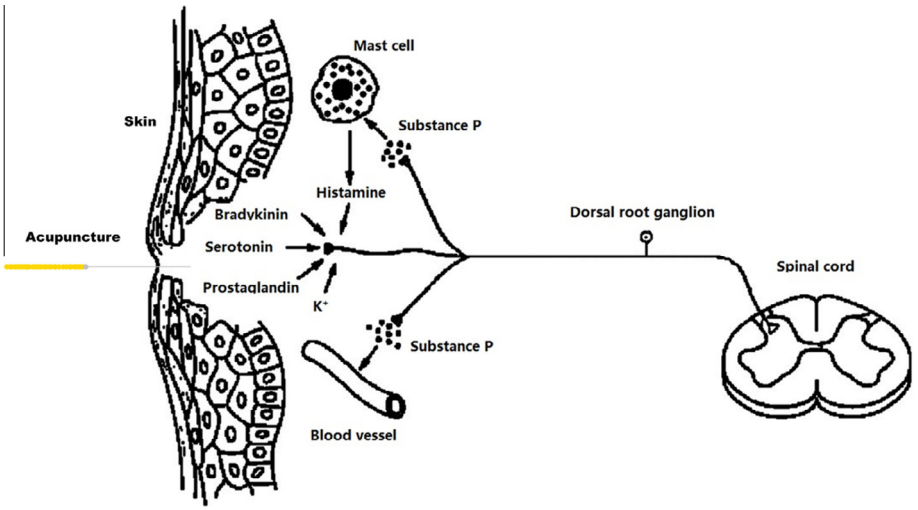

Fig. 1. Respond of receptors distributed in the skin evoked by acupuncture. When the nociceptors receive acupuncture stimulus, they can release chemical signaling factors, such as bradykinin, prostaglandin and serotonin [20]. Then action potentials are generated in a peptide-containing C fiber through tissue damage. In the end, they move along the axon of dorsal root ganglion cells, called pseudo-unipolar neurons, and to central branches.

including bradykinin and prostaglandin [20]. Then, it is send along dorsal root ganglion cells, called pseudo-unipolar neurons, to the central branch [20].

The characteristics of acupuncture neural electrical signals have been analyzed by nonlinear time series analysis [21,22] and complex network mapping [23]. Bayesian decoding algorithm has been used to deduce the type of acupuncture manipulation [24]. The establishment of feed-forward network model has promoted the investigation of the transmit channel for acupuncture signals [25]. However, these studies do not represent the stimulus–response relationship, i.e. how the acupuncture stimulus modulates the neural spike activities. Acupuncture manipulation in any types is composed of discrete stimulus events. In the neurophysiology experiments, only the stimulus times can be quantified so far and it is also the unique recorded feature of the stimulus. Therefore, acupuncture manipulation can be seen as an implicit stimulus and stimulus times are essential part for investigating the stimulus–response relationship. However, for unknown input stimuli, it is challenging to specify one model [26]. The state-space model introduces a signal analysis paradigm to analyze the response experiments of implicit stimuli [26]. So it is meaningful to represent the effects of different acupuncture manipulations by implicit state.

The state-space model is composed of an observation process and a state process. It is often applied to process continuous-valued data. When both observation process and state equation are known linear Gaussian, the Kalman filter can be used to estimate the model [26]. Furthermore, this algorithm has been extended when observation variables are point processes [26–30]. The expansion algorithm has great significance because the neural spike activities are usually recorded as point processes. Smith and Brown have summarized several advantages of state-space, in which we are most concerned is that the historical information of experiment and the temporal information of acupuncture manipulation are related to recorded spiking activities precisely by the implicit state [26].

The external stimulus drives the implicit process as a Gaussian autoregressive model to modulate neural spiking activities. The problem how to estimate the implicit state and unknown model parameters from the recorded random process has been solved by Smith and Brown [26]. Meanwhile the model goodness of fit to spike data has proved the rationality of model [26,31]. Here we establish the relationship between acupuncture stimuli and electrical signals in spinal dorsal horn neurons through state-space model and investigate how the different frequencies of acupuncture manipulations modulate neural spike activities. This is a preliminary exploration that why different acupuncture manipulations have varying effects. Coming up in Section 2, recorded neural spike activities are preprocessed by the sorting algorithm and then transformed into point process spike trains. In Section 3, the state-space model theory is introduced. In Section 4, both simulated data and real acupuncture data are studies with state-space model. Finally, the conclusion and discussion are given.

2. Signal acquisition and preprocessing

To better investigate the effects of acupuncture to healthy rats, their Zusanli points are stimulated by three different frequencies acupuncture manipulations (approximate 30, 60, 120 times per minute). Meanwhile, neural electrical signals of spinal dorsal horn neurons evoked by acupuncture are recorded by platinum electrodes. The spike train of each WDR neuron can be obtained by spike detection and sorting [32]. During detecting spikes, the threshold is set as