Norepinephrine suppressed bicuculline-induced bursting activity in cultured hippocampal neurons

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Abstract— Norepinephrine (NE) is considered to play a key role in effectiveness of vagus nerve stimulation. However, how it reduces epilepsy seizure is little known. To clarify the effect of norepinephrine, we induced epileptiform activity in cultured hippocampal neurons with bicuculline and applied NE to the culture. The analysis showed that an application of NE suppressed bursting activity which relates to epileptic activity.

I. INTRODUCTION

Norepinephrine is considered to be important in vagus nerve stimulation therapy [1][2]. However, there is little knowledge of the mechanism. Here we show the investigation of bursting activity in vitro, which is considered to be related to epileptic activity [3][4].

II. METHODS

Cell culture: Hippocampal neurons were dissociated from Wister rats (seven days old) and cultured for 65 days in an incubator. Half the culture medium was replaced twice a week.

Application of bicuculline (BCC) and norepinephrine (NE): The culture was set for 30 minutes for stabilization, and then 20 μM BCC was applied for 20 minutes, and 10 μM NE was applied for 20 minutes.

Spike detection: Extracellular potential signals were acquired with micro-electrode arrays with 64 electrodes and processed with band-pass filter (300-3000Hz). Absolute values of the negative peaks which exceeded the threshold $V_n = \sigma \cdot (\sigma = median \{|x|/0.6745\}, \ x$ denotes time series of extracellular cellular potential) were considered to be spikes.

Burst detection: Bursts were detected with an algorithm same to [5]. The parameters, the maximum expected ISI, the minimum number of consecutive spikes, were set to 3, 4 respectively.

III. RESULTS

Spikes of neurons with 20 μM BCC were concentrated temporally compared to those with 20 μM BCC and 10 μM NE (Figure 1. ). The burst analysis demonstrated that the number of bursts was reduced by an application of 10 μM NE (Figure 2. ). This result suggests that the effect of burst reduction by NE can be one of functions of NE that suppresses epilepsy seizures because bursting can be a model for deafferentation syndromes [4].

Figure 1. Extracellular cellular potential of hippocampal neurons with 20 μM BCC (A) before and (B) after an application of 10 μM NE. Activity pattern has changed after the application.

Figure 2. Number of bursts of hippocampal neurons with 20 μM BCC, and 20 μM BCC and 10 μM NE. The application of NE reduced the number of bursts approximately in half.

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REFERENCES