Biochemical and Biophysical Research Communications xxx (2016) 1–7

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Enhanced theta synchronization correlates with the successful retrieval of trace fear memory

Yujin Han [1], Bobae An [1, 2], Sukwoo Choi [*]

School of Biological Sciences, College of Natural Sciences, Seoul National University, Seoul, South Korea

A R T I C L E I N F O

Article history:
Received 14 September 2016
Accepted 25 October 2016
Available online xxx

Keywords:
Trace fear conditioning
Hippocampus
Theta synchronization

A B S T R A C T

Mechanisms underlying delay fear conditioning in which conditioned stimuli (CS) are paired and co-terminated with unconditioned stimuli (US), have been extensively characterized, thus expanding knowledge concerning learning and memory. However, trace fear conditioning in which CS and US are separated by trace interval periods, has received much less attention though it involves cognitive processes including timing and working memories. Various brain regions including the hippocampus are known to play an important role in memory acquisition and/or retrieval of trace fear conditioning. However, neural correlates, which are specific for the discrete steps in trace fear conditioning, have not been characterized thoroughly. Here, we investigated the network activities between the dorsal and ventral hippocampi at different stages of memory processing after trace fear conditioning. When fear memory was retrieved successfully, theta synchronization between the two regions was enhanced relative to preconditioning levels. The enhancement in theta synchronization was observed only during the trace interval period but not during CS presentation or after the trace interval period. Thus, the enhanced theta synchronization between the dorsal and ventral hippocampi may underlie a cognitive process associated with the trace interval period when fear memory is retrieved successfully.

© 2016 Elsevier Inc. All rights reserved.

1. Introduction

Fear conditioning can be categorized into two criteria based on the time interval between the conditioned stimuli (CS) and unconditioned stimuli (US): delay and trace fear conditioning. Delay fear conditioning involves the simultaneous presentation of a neutral tone (CS) and a noxious foot shock (US), and thereafter, presentation of CS alone induces conditioned fear responses during the presentation. In contrast, trace fear conditioning is a form of fear conditioning in which an interval (a trace interval period) is interposed between the termination of CS and the onset of US. Trace fear conditioning produces a robust fear response during CS presentation and during the trace interval period. Therefore, subjects appear to learn both an association between CS and US, as well as a temporal relation between them [1–3]. Importantly, the acquisition, storage, and retrieval of conditioned fear in trace fear conditioning are known to depend on various brain regions including the hippocampus [4–6]. However, it has not been thoroughly determined whether and how neurons in those regions respond to various stages in trace fear conditioning.

The ventral hippocampus is thought to be critical for stress, emotion, and affect, whereas the dorsal hippocampus appears to be involved primarily in cognitive functions including timing estimation [7–9]. Consistently, trace fear conditioning, which involves emotion and timing, requires both the ventral and dorsal hippocampi [1,10–12]. Synchronization of neuronal activities between multiple brain regions is frequently observed when their cooperation is required for proper behaviors [13,14]. Consistently, desynchronization leads to failure of adequate behaviors [15]. Therefore, it is possible that synchronization of neural activities between the dorsal and ventral hippocampi underlie trace fear conditioning that involves both emotion and timing. However, it has not been elucidated whether synchronization between the dorsal and ventral hippocampi exists during a specific stage in trace fear conditioning.

In the present study, we recorded local field potentials simultaneously from the dorsal and ventral hippocampi upon memory retrieval after trace fear conditioning in order to determine

* Corresponding author.
E-mail address: sukwoo12@snu.ac.kr (S. Choi).
[1] These authors contributed equally to this manuscript.
[2] Present address: Department of Neurobiology, Duke University, Durham, NC, USA.

http://dx.doi.org/10.1016/j.bbrc.2016.10.101
0006-291X/© 2016 Elsevier Inc. All rights reserved.

whether neural activities between the two brain regions are altered. In fact, both cross-correlation and phase coherence between the dorsal and ventral hippocampi were enhanced during the trace interval period upon memory retrieval.

2. Materials and methods

2.1. Animals

Male Sprague-Dawley rats (8 weeks old) were housed for 4–5 days before all experiments under conditions previously described [16]. All procedures were approved by the institute of Laboratory Animal Resources of Seoul National University.

2.2. Surgery and recording

Rats were anesthetized with sodium pentobarbital and maintained with isoflurane in oxygen (O_2). Rats were fixed on a stereotaxic frame and ipsilaterally implanted with electrodes targeting the dorsal hippocampal CA1 area (3.25 mm posterior, 2.50 mm lateral, and 3.00 mm deep from the bregma, left hemisphere) and ventral hippocampal CA1 area (5.50 mm posterior, 5.20 mm lateral, and 7.70 mm deep from the bregma, left hemisphere). The electrodes consisted of five individually insulated nichrome microwires (50 μm outer diameter; California Fine Wire, Grover Beach, CA, USA) and three stainless steel microwires (0.15 mm outer diameter; Plastics One, Roanoke, VA, USA) contained in a stainless steel guide cannula. A ground electrode was implanted above the cerebellum. Recording and ground electrodes were fixed to the skull by dental cement (Vertex Dental, Soesterberg, Netherlands). After surgery, rats were allowed to recover for a week. Neural activities were recorded using Plexon MAP system (Plexon, Dallas, TX, USA). Local field potentials were processed by a differential amplifier and band-pass filtered at 0.7 and 300 Hz with a 1 kHz sampling rate.

2.3. Behavioral procedures

The behavioral procedures used in the present study are summarized in Fig. 1B. A day before the procedures, each rat was handled for 5–10 min. On day 1, rats were habituated to the recording contexts (preconditioning and retrieval contexts) and the CS. Rats were placed in the preconditioning context (a rectangular Plexiglas box floored with a flat black Formica plate and illuminated with a red light) for 10 min, and then exposed to the retrieval context (a cylindrical Plexiglas box with a flat black Formica plate with a red light) for 10 min. The CS (30 s in duration, 2.8 kHz, 85 dB) was presented in the retrieval context 1 min before the end of exposure to the retrieval context. On day 2, rats were placed in the preconditioning context, and local field potential was recorded from the dorsal and ventral hippocampi while four CS were presented. CS presentation was initiated 3 min after the start of the preconditioning test and the interval between the CS presentations was 150–210 s. Then, trace fear conditioning was conducted in the same context as that of the preconditioning except that the chamber was floored with a metal grid and illuminated with a white light. CS was paired with an electrical foot shock that was separated by a 30 s trace interval period (US; 0.6 mA, 0.5 s, 10 CS/US pairings; intertrial interval: 150–210 s). Twenty-four hours after the conditioning (on day 3), memory retrieval was performed in the retrieval context and local field potentials were recorded from the dorsal and ventral hippocampi while four CS were presented. CS presentation was initiated 3 min after the start of the retrieval test and the interval between the CS presentations was 150–210 s. The freezing time during CS and trace interval periods was measured by trained observers. Freezing was defined as no movement except for respiratory activity. The total freezing time was normalized to the duration of the CS and trace interval period (30 s).

2.4. Data analysis

Local field potentials were analyzed using Neuroexplorer (Nex Technologies, Madison, AL, USA) and MATLAB (MathWorks, Natick, MA, USA). Signals obtained from an electrode, which has a clear signal and less noise in each region (dorsal and ventral hippocampi), were analyzed. To investigate the power of neural activity, power spectral density analysis was performed in a range of 2–20 Hz frequencies, normalized using a standard z-score transformation and averaged across animals in a designated group (success or failure group). Synchronization between the dorsal and ventral hippocampi was measured using cross-correlation analysis. All signals were band-pass filtered (4–8 Hz) and then cross-correlation between the two regions was calculated with ±0.5 s time lag of the dorsal hippocampal signal relative to the ventral hippocampal one. Cross-correlograms were averaged across animals. The second peak value of each cross-correlogram was considered as an index of correlation [17,18]. To analyze the phase coherence between signals from the dorsal and ventral hippocampi, local field potential data was imported into MATLAB for using custom-written software that was previously used [19]. Phase differences in the theta frequency (4–8 Hz) between two signals were measured by calculating the instantaneous phases of the two signals through the Hilbert transformation, and then subtracting them from each other. The results were then presented as histograms. The width of the histogram at half peak height was used as an index of phase coherence [19].

2.5. Histology

After all experiments, rats were anesthetized with urethane (1 g/kg, i.p.) and electrolytic lesions were made by passing a current (10 μA, 10 s) through recording wires. Then, rats were transcardially perfused with 0.9% saline solution followed by 4% paraformaldehyde in 10% buffered saline. Brains were removed and post-fixed overnight. Then, brains were sliced into coronal sections (100 μm thick) with a Vibratome (NVSL; World Precision Instruments, Sarasota, FL, USA). Slices were stained with cresyl violet and mounted on slides. The placement of implanted sites of electrodes was verified under a light microscope.

2.6. Statistical analysis

To compare the behavioral or electrophysiological results between the preconditioning and retrieval sessions, paired *t*-test was conducted. Differences were considered significant when the P-values were less than 0.05. Error bars indicate SEM.

3. Results

3.1. Simultaneous local field potential recordings in the dorsal and ventral hippocampi in rats undergoing trace fear conditioning

We recorded the local field potentials simultaneously from the dorsal and ventral hippocampi (the CA1 subfield of the two regions; Fig. 1A) using 13 adult rats with electrodes implanted in the two regions. The rats underwent trace fear conditioning as shown in Fig. 1B. A conditioned stimulus (CS; 30 s, 2.8 kHz, 85 dB) was paired with an unconditioned stimulus (US; 0.6 mA foot shock, 0.5 s), and CS and US were separated by a trace interval period (30 s). Freezing levels progressively increased and plateaued during the

Please cite this article in press as: Y. Han, et al., Enhanced theta synchronization correlates with the successful retrieval of trace fear memory, Biochemical and Biophysical Research Communications (2016), http://dx.doi.org/10.1016/j.bbrc.2016.10.101

Download English Version:

https://daneshyari.com/en/article/5505895

Download Persian Version:

https://daneshyari.com/article/5505895

Daneshyari.com