Interaction between basolateral complex of the amygdala and hippocampal CA1 in auditory fear conditioning effects on place cell activity

731.07

EJ Donzis, RL Rennaker & LT Thompson

Aging & Memory Research Lab., School of Behavioral & Brain Sciences, Univeristy of Texas at Dallas, Richardson, TX

Background

Place cells are hippocampal pyramidal neurons that preferentially fire when a rat enters a specific location. The place field in which a cell fires is established very rapidly and remains stable for several months. Several studies have shown the importance of sensory cues on place cell firing. Changes in the environment can cause partial remapping or total disruption of the place map. These changes can be physical or nonphysical that change the rat's perception of the environment. Our lab and others have shown that introducing a fearful stimulus into an environment causes remapping of place cells. The physiological mechanism for this remapping is unknown.

The basolateral complex of the amygdala (BLA) is anatomically and physiologically connected to hippocampus. Lesioning the BLA blocks memory enhancing effects of hippocampal activation and specifically spatial learning. It is therefore likely that the BLA modulates hippocampal plasticity induced by the fearful stimulus. During- and post-presentation of fearful stimuli, amygdalar neurons have increased firing rates. If this enhanced amygdala firing modulates hippocampal plasticity, then infusion of lidocaine into the amygdala immediately post-presentation of a fearful stimulus should attenuate hippocampal plasticity. The current study assessed these effects by examining plasticity of hippocampal place fields induced by fearful stimuli.

Hypotheses

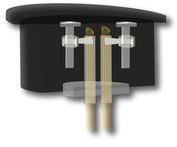
•Presentation of the CS **out**-of-field (i.e. during low firing rate) for a given place cell should not result in spatial remapping of that neuron's place field.

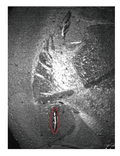
•When the CS is presented **in**-field (i.e. during high firing rate) for a given place cell, the rat should recall the aversive event associated with the CS and the new perceptual component should alter its spatial firing.

•If BLA activity modulates CS-induced plasticity of place cells, then blockade of the BLA by brief lidocaine infusion should attenuate CA1 place cell plasticity after CS presentation **in**-field.

Methods

Male Long Evans rats were implanted with recording electrodes consisting of multiple drivable tetrode bundles (right) in the CA1 of the hippocampus (fig. 1). In some rats, a cannula was implanted into the BLA (fig. 1). Rats were trained to explore all 8 arms of a radial-arm maze (below) for small appetitive rewards until stable unit activity was established using a Plexon MAP system. In a conditioning box, well isolated and differentiated from the maze environment, rats received 3 pairings of a 5 sec, 5 kHz CS tone with a 1 sec, 0.5 mA footshock. 24 h later, the rats were placed back on the radial-arm maze, and the CS tone was presented either while the rat was within the place field of a given unit or while the rat was exploring an area well outside of the place field. In the cannulated rats, lidocaine was infused into the BLA immediately after tone presentation on the radial arm maze. Place cell activity was recorded for multiple sessions up to 24 h after the tone presentation.





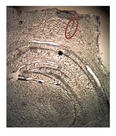


Fig. 1: Representative lidocaine inactivation site in BLA (left) and cannula track above CA1 from electrode (right).

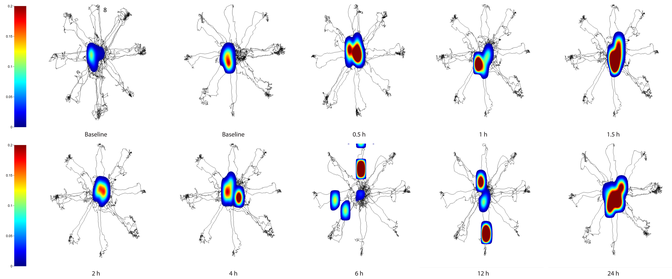


Fig. 2: Representative place field maps before and after CS presentation **outside** of the place field. The place field remained stable in the center of the maze with some changes noted 6 h and 12 h post tone presentation. 24 h post tone presentation, the place field remained in the center of the maze.

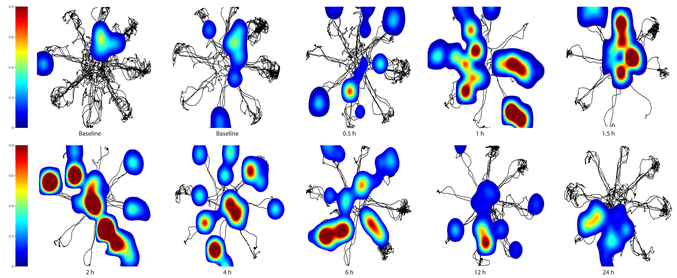


Fig. 3: Representative place field maps before and after CS presentation **in** the place field. Initially the place field was in the upper 2 arms. Immediately after the CS presentation, the place field was disrupted but by 6 h it began stabilizing in a new location. By 24 h, the old field was absent and a new field was stabilized.

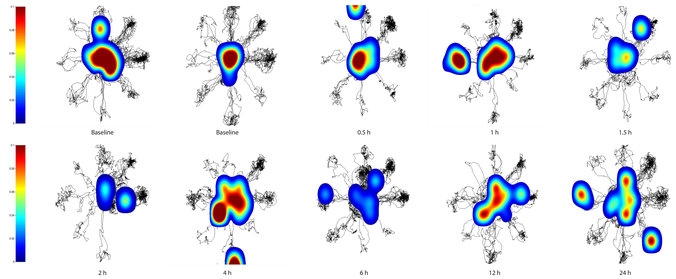


Fig. 4: Representative place field maps before and after tone presentation **in** the place field immediately followed by lidocaine infusion into the BLA. The place cell most frequently fired in the center of the maze in all recording session with some variability in out-of-field firing.

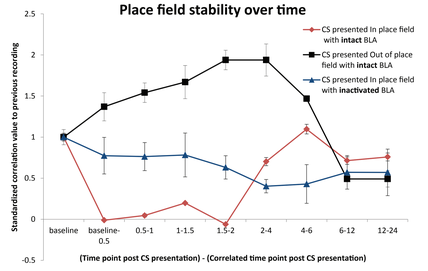


Fig. 5: Average standardized correlation values of the location of the current place map to the previous place map's location. The correlation values decreased 100% post CS presentation **in** the place field with an intact BLA but begin to stabilize 6 h post CS presentation. The correlation values increased 100% post CS presentation **outside** of the place field up to 4 h post CS presentation. BLA inactivation post-CS presentation **in** the place field attenuated the effects of CS presentation on the place field.

Results

•When the auditory CS was played out-of-field for CA1 place field, the place field became more stable up to 4 h post CS presentation then returned back to baseline stability at 12 h post-tone presentation and remained stable at 24 h (fig. 2 & 5).

•When the auditory CS was presented in-field, the place cells demonstrated diminished place cell stability within 30 min post CS presentation and remained unstable up to 4 h post CS presentation (fig. 3 & 5). Place field location had a low spatial correlation when compared to baseline recording sessions instead of the previous recording session (fig. 6).

•The stabilization of place fields compared to previous recordings but not baseline recordings suggests that the place fields re-stabilized in a new location. Presentation of the CS in-field followed immediately by an infusion of lidocaine into the BLA attenuated the effect of CS presentation in-field (fig. 4 & 5).

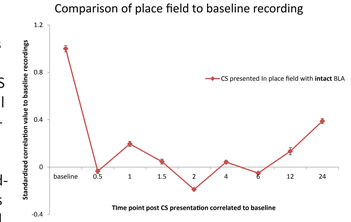


Fig. 6: Average standardized correlation values of the location of the current place map to the baseline location. The correlation decreased 100% immediately post CS presentation and never returned to baseline. The lack of correlation of the place map 24 h post CS presentation to baseline together with the data in figure 5 indicates that the place field stabilized in a new location.

Summary

•Presentation of a fear conditioned CS **outside** of the place field increased the stability of the place cell up to 4 h post CS presentation, i.e. did not change the location of the field.

•Presentation of a fear conditioned CS **in** the place field with an **intact** BLA initially disrupted the stability of the place field and resulted in the field moving to a new location.

•Presentation of a fear conditioned CS **in** the place field with an **inactivated** BLA attenuated the disruption of the place field due to CS presenation, i.e. did not change the location of the field.

Acknowledgements

This project was supported by grants from the Clark Foundation and American Tinnitus Association.