Comparative Nodal Analysis for Implicit Associative Learning Across Human and Non-human Primates

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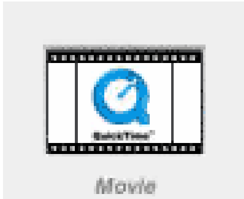
Introduction

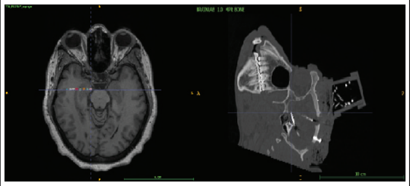
Elucidating the underlying neural mechanisms of experiential and associative learning is a central theme of neuroscience research (Corlett et al., 2004; Daniel and Pollman 2014; Downar et al., 2011; Shin et al., 2016). Temporal expectancy, a subset of associative learning, involves the implicit learning of temporal contingencies between the associated stimuli. It is known to be present starting in early infancy (Colombo and Richman 2002) and preserved throughout various species (Dallerac et. al, 2017). Thus, temporal expectancy learning may incorporate some of the most fundamental neural circuitry responsible for learning. The spectral dynamics of this network remain largely unknown, and no studies have performed comparative physiologic analysis between human and NHP species. We employed stereotactic electroencephelography to comparatively study neural network substrates underlying implicit associative learning in both humans and non-human primates (NHP) using the same temporal expectancy task.

Methods

Patients undergoing intracranial electrode implantation for seizure foci localization and two NHPs were included in this study. Subjects are shown a cue that changes color after a short delay with instruction to press a button following the color change. We used power spectral analysis to identify frequency bands related to task activity. We compared power in these bands between delay periods, reaction time, and early and late learning stages.

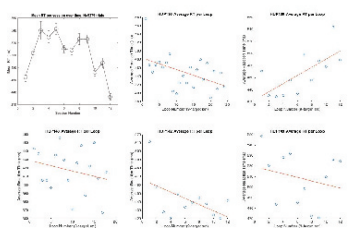


Hippocampal Electrode Localization



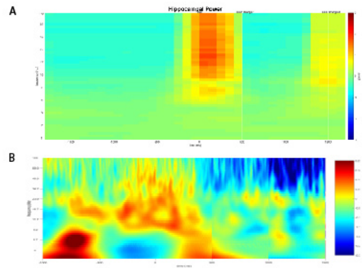
K>> Left: Coregistered MRI to post-implant CT. Example of Human stereotactic depth electrode targeting hippocampus. Right: NHP post-implant CT scan showing depth electrodes along long axis of hippocampus.

Subject Behavioral Data



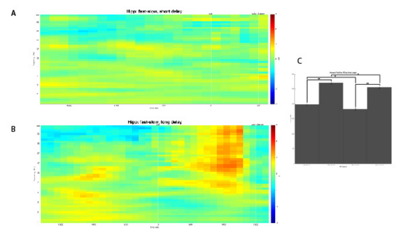
Averaged reaction time for NHP and human subjects over time.

Task-Related Power Spectral Density



A: Average task-related power spectral density of all human hippocampal contacts. B: Representative task-related power spectral density of NHP hippocampal electrodes.

Increased Hippocampal Power in Anticipatory Period of High Performance Trials



A & B: t-stats comparing power spectral density between trials with the fastest and slowest third of reaction times. Split by delay length. C: Average reaction times of fastest and slowest third of trials by delay length.

Results

We find broad spectral power increase between cue onset and first anticipated color change that dissipates, then reappears in a narrow frequency band before subsequent expected color change time points. This activity is preserved in NHPs and in human subjects. Performance-based analysis in human subjects reveals broad increased power before anticipated color change in high performance, long delay trials when compared to low performance trials with the same delay period. This effect is not seen in short delay trials.

Conclusions

1) Our results may implicate a role for the hippocampus in the performance of a simple temporal expectancy task.
2) Hippocampal activity in both humans and non-human primates is temporally linked to anticipated 'go' cue appearance.
3) Increased hippocampal activity prior to the go cue in the long delay period predicts faster reaction time in human subjects.

These results may provide evidence of preparatory activity in the hippocampus leading to superior task performance and similarities between human and non-human primate hippocampal activity may help to validate the primate model for use in a temporal expectancy task.

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