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Neurocomputing 32–33 (2000) 659–665

NEUROCOMPUTING

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Task dependence of human theta: The case for multiple cognitive functions

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Accepted 13 January 2000

Abstract

The recent finding of task-related theta oscillations in humans (M.J. Kahana, Sekuler, Caplan, Kirschen, Madsen, *Nature* 399 (1999) 781–784) raises a number of questions. We recorded from 345 intracranial electrodes in five patients with medically intractable epilepsy while they learned to navigate virtual mazes. Previously, we showed significant dependence of theta on two different task parameters, maze difficulty and study versus test modes. First, we show that these results hold for an additional 174 electrodes and two subjects, removing a previous confound between the two comparisons. Here we ask whether or not these two task parameters reflect some common, or correlated, task-correlates of theta. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Theta oscillations; Maze navigation; Intracranial EEG

1. Introduction

Theta (3–12 Hz) oscillations have long been observed in mammals during spatial navigation and are thought to be intimately involved in such tasks [2,6–13]. In recent work [3] our group demonstrated the relevance of theta to human brain function in a spatial navigation task. These results established the presence of theta in three epileptic patients and a significant relationship between the occurrence of theta and

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parameters of the task. One outstanding question concerns the nature of theta's role or roles in this task. Correlation maps revealed clusters of electrode locations showing strong covariance within cluster but weaker covariance between clusters. Could these relatively independent clusters reflect distinct functional roles that theta might play in this task? It may be possible to address this question by examining how theta varies with task parameters. Here we take the example of two such parameters which we have previously shown to vary with theta — task difficulty and *study* versus *test* modes [3]. Do these represent independent or correlated manipulations of task-related theta? If theta changes with more than one parameter, multiple parameters could all represent the same role or different roles. Through various approaches we examine the relationship between the sets of electrodes that exhibit each effect to answer this question.

2. Methods

2.1. Subjects and recording

We tested five patients with pharmacologically refractory epilepsy. To localize the epileptogenic focus, the patients had intracranial electrodes implanted for 1–2 weeks during which time seizure and functional data were collected. The placement of the electrodes was determined by the clinical team. We sampled a total of 345 electrodes (Figs. 1 and 2). Intracranial electroencephalographic (iEEG) signal was sampled at 200 Hz (Telefactor, band-pass filter: 0.5–100 Hz) for subjects 1–4 and at 256 Hz (BioLogic, band-pass filter: 0.3–70 Hz) for subject 5. The locations of the electrodes were determined by an indirect stereotactic technique [11].

2.2. Procedure

Subjects learned to navigate 3-D rendered, virtual, multiple T-junction mazes. Subjects traversed a maze four times in *study* mode, in which arrows were placed on the walls to reveal the correct path. Then subjects traversed the same maze in *test* mode, with the arrows removed, forcing them to rely on a learned representation of the maze. Subjects navigated a maze repeatedly until they traversed it three times consecutively without errors. Task difficulty was manipulated by varying maze length between short (6-junction) and long (12-junction) mazes.

2.3. Theta episode analysis

To analyze the spectral characteristics, we wavelet transformed the raw signal (Morlet wavelet, window = 6 cycles; [1]). A *theta episode* was defined as a duration longer than three oscillatory cycles throughout which the wavelet power exceeded $z = 1$ at a given frequency. The z -transform was based on the distribution of wavelet power at a given frequency across all windows in all maze trials in the experiment. For

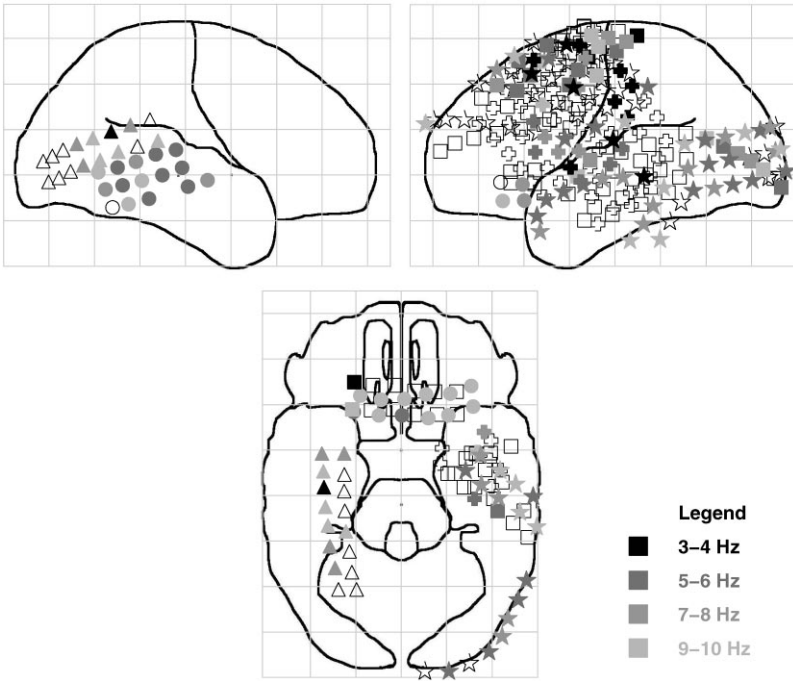


Fig. 1. Task difficulty effect. Electrode locations and task-dependent theta for all five subjects, shown on three sketched views (right lateral, left lateral and inferior) of a standard brain. Circles, triangles, squares, crosses and stars represent subjects 1–5, respectively. Filled shapes represent electrodes showing a significant ($p < 0.01$) maze-difficulty effect in the range 3–10 Hz; peak frequency is represented by grayscale (see legend).

a given trial, percent trial time in theta, P_θ , is the percentage of time during which theta episodes were present.

We compared P_θ across the two task manipulations using a two-tailed Mann-Whitney U -test. This was done at each central frequency separately over the range 3–10 Hz (1 Hz increments). For the summary topographic maps (Figs. 1 and 2), an electrode was denoted as showing an effect if it reached significance ($p < 0.01$) at *any* frequency within the range analyzed. The “peak frequency” denotes the frequency exhibiting the most significant p -value. The summary mean P_θ values quoted in the text represent a *union* of oscillatory episodes across all frequencies in the range 3–10 Hz.

List length has a profound effect on performance in human memory tasks [5,9,10]. The analogue in our task is the maze-length manipulation: long mazes were more difficult than short mazes for Brandeis undergraduates [4]. Another important functional distinction is made between encoding versus retrieval processes [12]. In our task this roughly corresponds to comparing *study* (arrow) trials with error-free *test* trials. We therefore analyzed theta activity in relation to both these task manipulations. Long mazes tended to require more test trials than short mazes, as well as

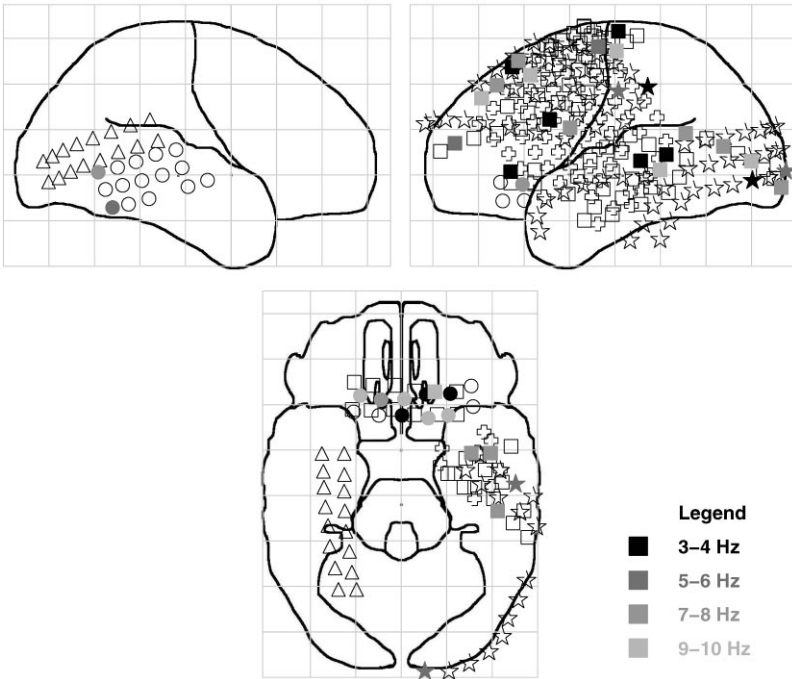


Fig. 2. Study/test effect (see Fig. 1). Note electrodes that show both effects (see text).

involving more errors (e.g., wrong turns). We therefore only included the first four study trials and last three (perfect) test trials in both comparisons to remove this confound. This put the two task comparisons on a similar footing, both involving analyses of the same set of trials, and removed trials in which maze length and study/test are correlated (imperfect test trials).

To look for pairs of electrodes that show correlated theta-band activity through the experiment, without reference to any specific task parameter we examined Pearson r correlations. These were computed across all pairs of electrodes within a subject for the timecourse of theta power over all maze trials. The unit of measurement was average wavelet power across the 3–10 Hz band while the subject was in a particular maze junction.

3. Results

First, we looked for electrodes that showed theta activity covarying with our two task parameters. Consistent with our previously reported results, for each patient the presence of theta oscillations covaried with maze difficulty; the percentage of a trial time occupied by theta episodes (P_θ) was significantly greater for difficult (12-junction)

than for easier (6-junction) mazes (Fig. 1) at many brain locations (151 out of 345, $p < 0.01$). No electrodes exhibited the reverse effect. For electrodes showing this effect, mean P_θ (including all frequencies in the range 3–10 Hz) was 8.6% for long maze trials and 5.5% for short maze trials. Likewise, for the study/test comparison, in 40 out of 345 electrodes, P_θ was greater in test than study trials ($p < 0.01$). For electrodes showing this effect, P_θ was 9.1% for test trials and 5.8% for study trials. For this comparison as well, no electrodes showed the reverse effect. For subjects 2 and 4, no electrodes were significant in the study/test comparison; hence, we focus on the three subjects who had electrodes showing both effects.

3.1. Common electrodes

A subset of electrodes showed both task dependencies (e.g., in the inferior frontal region of subject 1 and in the occipital strip of subject 3; see Figs. 1 and 2). If membership in one group were independent of membership in the other, one would expect some overlap by chance,

$$N_{\text{total}} \frac{N_{\text{length}}}{N_{\text{total}}} \frac{N_{\text{study/test}}}{N_{\text{total}}}.$$

For the three subjects where we see a study/test effect, the observed overlaps were not significantly different from chance levels, even when we collapse across subjects ($\chi^2(2) = 2.79, N = 40, p = 0.25$). Hence, at this stage we could not reject the hypothesis that the two sets of electrodes represent independent comparisons. However, if the two task manipulations influence a common process or correlated processes then for electrodes showing only one effect, the non-significant effect might simply lack the statistical power to pass the significance threshold. This appears to hold; when we repeat the χ^2 analysis just described, but using an initial threshold criterion of $p < 0.1$ instead of $p < 0.01$ the overlap between the effects is significantly greater than expected by chance ($\chi^2(3) = 12.0, N = 122, p < 0.01$). Note that here we exclude subject 1, who shows all 31 electrodes significant for the maze difficulty effect and we include subjects 2 and 4 (previously excluded) because at this threshold they have electrodes showing both effects. This argues that the two task dependencies are *not* tapping independent theta-relevant task variable and that the previous χ^2 result was due to a thresholding artifact.

3.2. Peak frequencies

An alternative account is that the maze length and study/test parameters influence properties of theta differently at the same brain locations, for example, different frequencies of oscillations. The median peak frequency did not differ between the two effects for subjects 1 or 3. For subject 5 (across electrodes showing both effects) the peak frequency was 2 Hz lower for the study/test than for the maze difficulty effect ($p < 0.01$). Further, the three electrodes in subject 5 showing both effects all differed in the same direction. Note that peak frequency varies considerably across electrode

locations as well as across subjects, which limits our ability to draw inferences from this line of analysis.

3.3. Correlations

Finally, the topography of correlations across the whole experiment suggests that theta activity frequently co-occurs in electrode pairs within a region but less so for pairs that cross obvious anatomic boundaries. If these clusters indicate independent roles for theta, we can ask whether the electrode clusters selected by the two task parameters are related to these. Considering only electrodes showing exactly one of the two effects, we compared the mean Pearson r for electrode pairs that both showed the same effect (r_1 and r_m , maze difficulty and study/test mode effects, respectively) with the those for pairs that each showed different effects (r_{1m}). The values for r_1 , r_m and r_{1m} were 0.25, 0.28 and 0.24 for subject 3 and 0.23, 0.15 and 0.18 for subject 5. For subject 3, only r_{1m} and r_m differed at borderline significance ($p = 0.057$); for subject 5, only r_{1m} and r_1 differed significantly ($p < 0.001$). Hence, the agreement between these two task parameters the clustering observed in the correlation maps is suggested, but not solid. These two task manipulations do not relate strongly to the correlation map clusters.

4. Discussion

We investigated the novel hypothesis that human theta has multiple cognitive roles. As an example, we tested this in relation to two particular task parameters. We first replicated our original findings [3], showing maze difficulty and study/test effects across twice as many electrodes as before (345 versus 171) including two additional subjects, and eliminated a potential confound between the two manipulations. This allowed us to assess whether the two task parameters influence theta in independent ways. The number of electrodes showing both effects did not differ significantly from chance but this was probably due to a significance-thresholding artifact. We were unable to find decisive evidence that these two task parameters affected theta in a separable way. By applying analyses like those presented here to the numerous other parameters of this task it will be possible to further constrain the possible roles that theta has in human cognition.

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