ENHANCED GAMMA (30–150 Hz) FREQUENCY IN THE HUMAN MEDIAL TEMPORAL LOBE

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Abstract—We performed fast Fourier transformation power spectral analysis of the electrocorticogram in human medial temporal lobe during wakeful rest in six epileptic subjects. Compared with the electrocorticogram wave in the basal temporal lobe, which showed monotonic decline of spectral power across the frequency axis, the electrocorticogram wave in the parahippocampal gyrus was enhanced (or did not decline) in the gamma frequency range (30–150 Hz) in all subjects.

Although it has been suggested that electrical oscillations of the hippocampus have functional roles in higher brain functions, namely learning and memory, the knowledge of hippocampal oscillations is largely limited to animal studies. The present results demonstrate that fast frequency oscillation is also present in the human medial temporal lobe, which has been reported in animal hippocampi. They also demonstrate the importance of recording very fast field potentials in human electrocorticograms. This fast oscillation is likely to play important functional roles related to learning and memory, possibly to induce long-term potentiation in the human medial temporal lobe. © 1999 IBRO. Published by Elsevier Science Ltd.

Key words: gamma oscillation, human medial temporal lobe, parahippocampal gyrus, hippocampus, electrocorticogram, spectral analysis.

The hippocampus has long been known to have mnemonic functions in both humans and animals. Almost a century ago, von Bechterew reported a patient with bilateral softening of tissue in the hippocampus and amygdala who manifested severe memory disturbances (see Ref. 36). Human patients with hippocampal lesions have been studied extensively,7,16,36 and theories have been tested experimentally in well-localized hippocampal regions in rats21,23,24 and monkeys.19,27 These studies have revealed important functional differences in the role of limbic structures in memory processes.8

The functional involvement of the hippocampal region in memory has attracted the interest of neuroscientists seeking neurophysiological correlates of memory functions. It has long been known that regular hippocampal theta activity is present during exploratory behavior,13,15 and during rapid eye movement sleep periods in both cats14 and dogs.25 Recently, it was suggested that theta field potentials are related to long-term potentiation (LTP), a possible neurobiological basis of memory.29 It is also of interest that faster (gamma) oscillations have been found in the hippocampus.18 It has been suggested that these oscillations have functional roles in cerebral information processing (see Ref. 12 for review). Nevertheless, the electrophysiological properties of the human hippocampus have been barely understood.

We recorded electrocorticograms (ECoGs) from electrodes on the parahippocampal gyrus and basal temporal cortex in epileptic patients.

EXPERIMENTAL PROCEDURES

Subjects were six patients (five male and one female; age 25–47 years) who were candidates for neurosurgical treatment of temporal lobe epilepsy. No visually definite atrophy of either hippocampi was identifiable in any subject by magnetic resonance imaging examination prior to surgery. Recordings were carried out approximately one week after surgical placement of subdural electrodes, when continuous video epileptic convulsion monitoring had been fulfilled. On the day of recording, each patient was fully alert and able to perform daily living activities (e.g., talk, walk, eat and use toilet by themselves).

Subdural electrodes were attached to cortical areas and the parahippocampal gyrus exclusively for the clinical purpose of evaluating the foci of epileptic seizures. Specially designed T-shaped sets of eight electrodes were attached to record parahippocampal and basal temporal cortical activities from both hemispheres (Fig. 1A).26 Four electrodes were attached along the long axis of the parahippocampal gyrus and the other four were attached across the base of the temporal lobe on each side to record ECoGs.

In addition to ECoGs, a Cz-A1 scalp electroencephalogram (EEG), an oblique electro-oculogram and a
chin electromyogram were recorded to monitor the state of consciousness. All signals were recorded on either a TEAC XR-9000 28 channel FM analog tape recorder, TEAC SR-8000 or Sony SIR-1000 32 channel digital recorders. Data recorded on analog tape were digitized at or above 1500 Hz and the sampling rate was further reduced with a finite impulse response (FIR) high cut filter (cut-off frequency 300–350 Hz) to obtain 750-Hz digital data. Data on digital tape were similarly sampled at 3000 Hz or above, then down-loaded onto a computer hard disk, and 750-Hz data were obtained using the same methods applied to analog data. We analysed signals from three parahippocampal montages and three basal temporal montages (H1, H2, H3 and T1, T2, T3 in Fig. 1B) on both sides during resting wakefulness with eyes closed. Fast Fourier transformation was performed on 50 1024-point (1.37 s) epochs. These 68.27 s of artifact and epileptic discharge-free ECoG signals were visually selected for statistical analyses. Every two fast Fourier transformation frequency bins were summed to obtain frequency bins 1.46 Hz wide. Power spectra from each pairing of the six derivations were compared for each 1.46-Hz bin for each subject, using the Mann–Whitney U-test.

This protocol was approved by the Tokyo Institute of Psychiatry ethical committee. A written informed consent was obtained from each patient prior to the recording.

**RESULTS**

A representative subject’s raw parahippocampal (left H3) and basal temporal (left T3) signals and 30–150 Hz FIR band-pass filtered waves are shown in Fig. 2. The parahippocampal signal exhibits continuous fast activities, as compared with the signal from the basal temporal ECoG.

Figure 3C presents spectra from the posterior part of the left parahippocampal gyrus (H3) and left lateral basal temporal lobe (T3) of the same subject as in Fig. 2. T3 of the ipsilateral basal temporal lobe was chosen for comparison since it was most distant from the hippocampus and considered to be less influenced by hippocampal field potentials. The H3 signal showed significantly higher activity, from 28 to nearly 250 Hz, with a 30–150 Hz band showing characteristic enhancement (Fig. 3C). In this patient,
Fig. 3. Power spectrum of one case of gamma enhancement in the posterior parahippocampal gyrus. Thick lines are power spectra from parahippocampal gyrus; the thin line is from the ipsilateral basal temporal derivation (T3). The shaded area indicates significant differences (Mann–Whitney U-test, $P < 0.05$) between parahippocampal gyrus and basal temporal power. Although significant differences were also present in wider bands, 30–150 Hz enhancement was significant in the H2 and H3 derivations.
Fig. 4. Power spectrum of one case of gamma enhancement in the anterior part. Thick lines indicate parahippocampal and thin lines indicate basal temporal spectra, as in Fig. 3. Note that 30–150 Hz is enhanced in the anterior part (H1). The shaded area indicates significant differences (Mann–Whitney U-test, $P < 0.05$) between parahippocampal and basal temporal power. There were significant differences between H3 and T3 in almost all frequency bands. However, the shapes of the spectral curves were similar and neither showed a specific enhancement in the gamma band.
discussion

In ECoG recordings from the human parahippocampal gyrus, spectral power in the 30–150 Hz band is significantly enhanced relative to the power in the basal temporal cortex of awake subjects. To the best of our knowledge, this is the first report of high-frequency ECoG enhancement in the human medial temporal lobe. It was difficult to precisely identify the enhanced frequency in the ECoG from the parahippocampal gyrus compared with the lateral basal temporal ECoG, because of cross-montage and inter-subject variations in general signal levels. However, the shapes of the spectral curve allowed us to determine that the ECoG power in 30–150 Hz is enhanced in signals from the parahippocampal gyrus compared with those from the lateral basal temporal lobe. Since this band coincides with gamma frequencies, we refer to this band as gamma.

In the past, we have studied human EEG oscillations during sleep. We focused on EEG oscillations (over a wider time-scale), since we believe they are correlates of certain brain functions by the following rationale. It is known that some neurons show rhythmic firing. However, even when a single neuron shows rhythmic firing, oscillatory field potentials (EEG) will not be observed without synchronous rhythmic activity of a substantial population of neurons. Therefore, observed EEG oscillations reflect mass neuronal activity in the brain. It is quite likely that such mass activity is importantly related to brain functions. Thus, we believe the local gamma frequency represents function(s) in the human medial temporal lobe.

Buzsaki et al. reported that, in rats, hippocampal fast rhythms of 25–100 Hz increased with behavioral activation. Similar frequencies are also enhanced in rats after locally induced after-discharge in the hippocampus. The spectral pattern of the present spontaneous activity from human parahippocampal gyrus closely resembles the pattern of enhancement by after-discharge in the rat hippocampus. Although the frequency is higher in humans, this similarity may still indicate that these frequencies reflect similar functional roles, although these roles remain unknown. This similarity also suggests that the signals recorded from the parahippocampal gyrus strongly reflect hippocampal activity.

Bragin et al. reported that gamma (40–100 Hz) field potentials are present in the hippocampus of the behaving rat. They suggested that gamma oscillations are generated by an interaction between intrinsic oscillatory properties of interneurons and the network properties of the dentate gyrus. The 40–100 Hz frequency they reported largely overlaps that identified in the present report. Although we must be cautious in our interpretations because of differences in our methods (we recorded field potentials and they used microelectrodes), comparisons of these data could prove useful.

In some cases, frequencies above 150 Hz were also relatively enhanced in the parahippocampal ECoG compared to the basal temporal cortex. This could be caused by average differences in signal levels between the H3 and T3 derivations. However, it is also possible that activity in the parahippocampal gyrus per se is enhanced up to 300 Hz. Enhanced spectral power above 150 Hz might correspond to the 200-Hz high-frequency network oscillation found in the CA1 region of rats. In any case, the existence of such high-frequency oscillation suggests that it plays a role in inducing LTP in the human medial temporal lobe.

The current finding that gamma frequency is enhanced in the signals from the human parahippocampal gyrus has basic and clinical implications. One of the most basic questions is why this region has a power spectrum which differs significantly from the basal temporal lobe. Since the parahippocampal and hippocampal region has anatomically different structures from the neocortex, the difference in spectral power could relate to these anatomical differences. It would be of interest to determine whether this is a general difference between three-layer and five-layer cortical structures, and whether it is regionally specific. It is possible that other regions of the cerebral cortex have these oscillations. Recently, it was reported that EEG 30–70 Hz oscillatory activity is induced by a visual search task in humans. We are currently accumulating ECoG data during task performance and hope to provide data relating human gamma oscillations to task performance. Although we
described 30–150 Hz as a single frequency band in this paper, task studies may reveal that this can be divided into discrete functional frequency bands.

There were differences in the level of gamma frequency enhancement across the parahippocampal gyrus and among individuals. Two cases showed higher gamma in the posterior part of the parahippocampal gyrus; two cases showed higher gamma in the posterior and the anterior part of the other. Enhancement locations were not identified in the remaining two subjects because of an insufficient number of readable (artifact-free) electrode placements. We can think of several possible explanations for these differences. One is that, because we recorded the difference in signals between two electrodes located on the parahippocampal gyrus, synchronized oscillatory signals could be weak. This can be resolved by recording signals using a common extra-hippocampal reference. We are currently accumulating such recordings. The second possibility is that epileptic focus in the hippocampus has not functioned normally. Such regions may not generate much gamma activity. If regional differences in gamma activity are caused by epileptic foci, gamma activity levels might predict residual hippocampal functioning. Such information could be valuable for anticipating postoperative deficits in brain function, allowing clinicians to better explain risks to the patient and to plan treatment procedures. In functional magnetic resonance imaging studies, it was reported that the posterior medial temporal lobe was activated during memory performance. In our present results, six of eight medial temporal lobes (both sides from four subjects) showed posterior enhancement. Taken together, it may be suggested that anterior enhancement occurred to substitute posterior function, which had been impaired by epileptic pathology.

The extent of coherence of activity in the hippocampal region and other cortical regions would be of further interest. If the present gamma oscillation has roles in both LTP induction and cortical information binding, it would be of great interest. Since the brain works as a system, such measures could lead to an understanding of the role of the hippocampus in overall brain function. Such data could ultimately help us understand pathological (e.g., schizophrenia) as well as physiological brain function.

CONCLUSIONS

In ECoG recordings from the human parahippocampal gyrus, spectral power in the 30–150 Hz band was significantly enhanced relative to the power in the basal temporal cortex in awake subjects. These results demonstrate that fast frequency oscillation is also present in the human medial temporal lobe, which has been reported in animal hippocampi. They also demonstrate the importance of recording very fast field potentials in human ECoGs. This fast oscillation is likely to play important functional roles related to learning and memory, possibly to induce LTP in the human medial temporal lobe.

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