Evoked potentials of parahippocampal gyrus in memory recovery

Potenciales evocados del giro parahipocampal en la recuperación de la memoria

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ABSTRACT

Findings from functional imaging and lesion studies have suggested that the hippocampus and the parahippocampal gyrus play an important role in short-term memory formation and its retrieval. However, there has not been enough evidence to validate this idea in terms of an electrophysiological approach. We recorded the event-related potential (ERP) in the parahippocampal gyrus of a patient with lateralized memory function, which supports the contribution of this region to memory retrieval. Conventionally, the medial temporal lobe has been considered necessary for long-term memory encoding, but not for short-term maintenance of items in working memory (WM) because patients with medial temporal lesions are not impaired in simple WM tasks involving maintenance of single items. The purpose of this paper is to present the unusual case of an ERP in the parahippocampal gyrus after gamma knife (GK) radiosurgery and its implication on WM.

Key words: Hippocampus. Medial temporal lobe. Long-term memory. Working memory. Parahippocampal gyrus.

RESUMEN

Los resultados de estudios funcionales de imagen y de lesiones han sugerido que el hipocampo y la circunvolución parahipocampal desempeñan un papel importante en la formación de la memoria a corto plazo y en su recuperación. Sin embargo, no ha habido suficientes pruebas para validar esta idea en términos de un enfoque electrofisiológico. Nosotros registramos un potencial evocado relacionado a recuperación (PERP) en la circunvolución parahipocampal de una paciente con memoria lateralizada, lo que apoya a la contribución de esta región en la recuperación de la memoria. Tradicionalmente, se ha considerado al lóbulo temporal medial (LTM) como necesario para la codificación de la memoria a largo plazo (MLP), pero no para el mantenimiento a corto plazo de los elementos en la memoria de trabajo (MT), ya que los pacientes con lesiones temporales mediales no se ven afectados en las tareas de la MT que implican el mantenimiento de los distintos elementos. El propósito de este trabajo es presentar el caso inusual de un PERP en la circunvolución parahipocampal después de radiocirugía con gamma knife (GK) y su implicación en la memoria de trabajo.

Palabras clave: Hipocampo. Lóbulo temporal medial. Memoria a largo plazo. Memoria del trabajo. Parahipocampo.

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INTRODUCTION

Several authors have reported that working memory (WM) has been conceived and defined in three different, slightly discrepant ways: as short-term memory applied to cognitive tasks, as a multi-component system that holds and manipulates information in short-term memory, and as the use of attention to manage short-term memory¹⁻⁴. Many functional magnetic resonance imaging (fMRI) studies analyzing and documenting WM load have focused on the prefrontal cortex (PFC) and have proven the increment in activity in this area with increasing load⁵.

Different models of WM have suggested a mechanism by which a persistent spiking at the cellular level could be used to hold various items in a WM buffer^{6,7}. These mechanisms may also be critical for maintaining new data through a delay and may allow multiple elements to be attached to each other through time⁸. Thus, some of these models focus on WM in the medial temporal lobe (MTL) regions instead of the PFC⁷. These studies used stimuli such as faces and words⁹ or letters¹⁰, which were strongly familiar to the subjects, and did not report activity in the MTL.

In contradiction, recent fMRI studies suggest that stimuli are trial unique, the MTL regions are recruited to maintain this novel information^{11,12}. Moreover, this delayed activity is related to long-term memory (LTM) encoding¹¹. These results are consistent with neurophysiological recording and functional mapping studies of WM in animals^{13,14}. Furthermore, neuropsychological studies in humans have shown that MTL is essential for WM with new information even for memory delays¹². Computer modeling has also predicted that MTL regions are crucial for the maintenance of trial-unique stimuli and could be modulated by WM load^{7,15,16}.

Radiosurgery

Epilepsy surgery is an effective treatment for medically resistant temporal lobe epilepsy (TLE) and is considered an invasive treatment. To minimize complication rates and potentially improve neuropsychological outcomes for medically intractable epilepsy, stereotactic radiosurgery (SRS) has been explored as an alternative method. Indirect evidence of the antiepileptic effect of SRS has been found in the treatment of tumors and arteriovenous malformations^{17,18}. SRS has been suggested as an effective therapy for drug-resistant epilepsy, with the

potential of having lower morbidity than resection, as well as its minimally invasive nature¹⁹⁻²¹. Two pilot trials have demonstrated the effectiveness of SRS for the treatment of medically resistant TLE, with a seizure-free outcome of approximately 65% at last follow-up^{19,20}. In the case presented here, it was not an effective treatment.

Histopathology

Vale et al.²² and Kawai et al.²³ reported neuropathological examinations of the mesial temporal lobe after gamma-knife (GK) radiosurgery. The hippocampus and surrounding structures showed prominent astrogliosis, acute and chronic hemorrhage, and/or blood extravasation. There was an evidence of radiation injury to the vascular walls and endothelial cells, with associated inflammatory and reparative changes. In addition, there was a moderately severe, remote, long-standing sclerosis at the level of the hippocampus. Pyramidal cell neuron loss was demonstrated mainly at CA4 (95%), CA3 (90%), proximal CA1 (80%), and the Sommer sector (80%), but CA2 cells were relatively preserved. These authors also reported severe damage in the entorhinal region, inferolateral to the hippocampus, with characteristic features of radiation injury: hemorrhage and blood extravasation, hemosiderin deposition, radiation vasculopathy, brain parenchymal necrosis, astrogliosis, rarefaction, and neuronal loss.

Subdural electrodes

Shimizu et al.²⁴ have documented the use of subdural electrodes that have a slender trapezoid shape and are easily introduced to the inner uppermost portion of the parahippocampal gyrus. Their results have shown that mesial temporal electrodes can detect not only interictal spikes but also subclinical and clinical seizure discharges from the mesolimbic structures, and they have excellent capability for lateralization of the mesial temporal epileptic focus. If mesial temporal subdural strips are used in combination with lateral temporal subdural grids, comprehensive understanding of the focus distribution throughout the temporal lobes will be possible without using depth electrodes. In the case here presented, we have used these subdural electrodes following the procedure of Dr. Shimizu.

CASE PRESENTATION

We report the case of a female patient presenting epileptic seizures from the age of 2 years. In 2006, when

Figure 1. Subdural electrodes implanted.

she was 42 years old, she was treated with GK radiosurgery for a left TLE in another hospital, with unfavorable results. Three years later, she was admitted to our hospital for intracranial electroencephalography (iEEG) and surgery. The Wada test showed right dominance in memory function.

For iEEG, we used trapezoid-shaped electrode sheets on which eight platinum electrodes were arranged in a “T” shape. The sheets were inserted so that the four small electrodes were aligned longitudinally to the parahippocampal gyrus²⁴⁻²⁶. The diameter of each electrode was 1.5 mm and interelectrode interval was 5 mm (center to center) (Unique Medical, Tokyo, Japan) (Fig. 1). Visual stimuli were presented using a monitor placed at a distance of 100 cm from the patient, using a stimuli output sequencer (light NoruPro Systems Inc., Tokyo, Japan). We performed video EEG, electrocorticogram (ECoG), MRI, CT scan, positron emission tomography (PET), and single-photon emission computerized tomography (SPECT) for diagnosis.

Experimental paradigm

- The patient was requested to perform two different tasks while we recorded an ECoG, similar as reported and validated by Axmacher et al.²
- The first was the picture-naming task, in which we showed 100 pictures, consisting of 42 different pictures in a random order, and the patient was required to name the objects
- Following the picture-naming task, we presented in a random order 10 of the 42 pictures used in it. The patient was requested to name silently each presented picture, and the patient attempted to remember

Figure 2. Picture naming (left) and memory task (right).

them for 3 min (encoding time). After 15 min, we conducted the memory task showing 100 pictures (the same ones used in the picture-naming task) but in a different order (Fig. 2); the patient was requested to push a button each time that a presented picture was recognized as one of the target pictures.

Recordings and analyses

- The ECoG was amplified and digitally recorded at sampling rates of 400 Hz
- We used a bandpass filter between 0.1 Hz and 120 Hz and a noise filter between 49 Hz and 51 Hz. We excluded trials with epileptic discharges and significant noise before the analysis of the averaging process
- We obtained event-related potential (ERP) with the picture-naming task (pic-ERP) and memory task (mem-ERP) by averaging the preprocessed data
- To obtain the ERP, which is relevant to retrieving memory function (ret-ERP), we subtracted mem-ERP from pic-ERP
- Analysis of all the data was performed using EMSE (ver. 5.3, source signal imaging, San Diego, CA).

Differential diagnosis

We confirmed the diagnosis of MTLE by video EEG, ECoG, MRI, CT scan, PET, and SPECT.

Surgical treatment

The surgical procedure used for the treatment of TLE was a left transsylvian selective amygdalohippocampectomy^{27,28}, for non-dominant side language.

Figure 3. Retrieval ERP (left and right parahippocampal gyrus).

RESULTS AND FOLLOW-UP

There was a large negative deflection ranging from 400 to 700 ms (Fig. 3).

The peak latency was around 600 ms.

At present, 4 years later, the patient is seizure free (Engel I).

Ethical considerations

This study was in accordance with the 2008 revision of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of University of Tokyo Hospital, and we also obtained the informed consent from the patient.

DISCUSSION

We have seen the activation (ERP) of the right parahippocampus and the absence of activity in the left parahippocampus gyrus (Fig. 4); this lateralization is strongly suggested to be the effect of the GK radiosurgery.

The most interesting finding was the 600 ms that was the time of activation of the right parahippocampus during both tasks through the averaging and subtraction between the memory test and picture naming (Fig. 3).

3D-brain Surface with ret-ERP projection

Figure 4. Activation (ERP) of the right parahippocampus.

Furthermore, the amplitude was larger on the anterior part of the right parahippocampal gyrus than on the posterior part, and likewise, from the medial to the lateral gyrus, suggesting a greater electrophysiological activity in the anterior than in the posterior hippocampus area.

In a recent study using iEEG recordings, Axmacher et al. also observed an increasingly negative potential during the maintenance of multiple items¹⁻³.

Axmacher et al.², in an experiment using WM load, induced more negative late hippocampal ERP components, suggesting that the hippocampus is not only crucial for LTM encoding but also plays a role in WM as well. Particularly, it has been shown that the hippocampus is

important for WM maintenance of multiple items or associations between item features.

Brewer et al.²⁹ and Gabrieli et al.³⁰ performed fMRI scans reporting evidence for the participation of the MTL in the encoding of memories. The most consistent locus of activation occurred bilaterally in the parahippocampal cortex, a major component of the MTL system, similar to what occurred in our patient; however, in our case, we placed subdural electrodes in both parahippocampus gyri, and only the right parahippocampus cortex was activated.

Probably, the time-frequency analysis could provide us with more information about the encoding of memory in the parahippocampal cortex and hippocampus.

CONFLICTS OF INTEREST

None.

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The authors declare that they have not received funding for this study.

ETHICAL DISCLOSURES

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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