Left hippocampectomy in an epilepsy patient with right hemisphere language dominance

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Abstract: Background: The left hippocampus is believed to play an important role in memory function. Thus, left hippocampectomy should be carefully performed. However, the left hippocampus may be less important for memory in patients with right hemisphere language dominance. We performed left hippocampectomy in a patient with epilepsy and right hemisphere language dominance. Here we present the findings of our functional mapping and examine the relationship between memory and language dominance.

Methods: The patient was a 32-year-old left-handed female implanted with subdural electrocorticography (ECoG) grids over both hemispheres to locate the epilepsy focus. Language dominance was determined by the Wada test. Functional localizations were identified with ECoG and electrocortical stimulation (ECS) mapping. The Wechsler Memory Scale-Revised (WMS-R) was used to evaluate the patient's memory before and after surgery.

Results: The epilepsy focus was located in the left mesial temporal lobe and hippocampus. The Wada test revealed right hemisphere language dominance. High gamma activity (HGA) mapping was consistent with ECS mapping in that both showed language-related activity in the right precentral gyrus. The WMS-R revealed improved memory after left hippocampectomy, without neurological deficits. The patient fully recovered without further epileptic seizures.

Conclusion: Left hippocampectomy in a patient with epilepsy and right hemisphere language dominance did not cause memory...
dysfunction. Thus, memory function is possibly related to the language-dominant hemisphere. Furthermore, preoperative mapping and determining a patient’s language dominance can help to preserve language and memory in epilepsy surgery.

**Subjects:** Medical Imaging; Epilepsy; Neurosurgery

**Keywords:** memory; hippocampectomy; language dominance; electrocortico gram; high gamma activity

1. **Introduction**

Mesial temporal lobectomy including the hippocampus is a common procedure in epilepsy surgery (Wieser, 1988). However, left hippocampectomy should be carefully performed because it often leads to memory dysfunction (Alpherts, Vermeulen, van Rijen, da Silva, & van Veelen, 2006; Berenbaum, Baxter, Seidenberg, & Hermann, 1997; Helmstaedter, Roeske, Kaaden, Elger, & Schramm, 2011). Although multiple subpial transection (MST) of the hippocampus has been noted for preserving memory function, the surgical procure is not the gold standard therapy in epilepsy surgery (Faught, 2002; Shimizu, Kawai, Sunaga, Sugano, & Yamada, 2006). Left hemisphere language dominance is common and reported in at least 90% of patients, whereas absolute right hemisphere language dominance is rare and reported in less than 10% of patients (Hardyck & Petrinovich, 1977; Knecht, Deppe, et al., 2000; Knecht, Drager, et al., 2000; Pujol, Deus, Losilla, & Capdevila, 1999). It is possible that patients with right hemisphere language dominance show similar lateralization for memory function. In this report, we present a patient with right hemisphere language dominance who suffered from left mesial temporal epilepsy. We performed functional brain mapping and using the Wada test to determine the language-dominant hemisphere, electrocorticography (ECoG) and electrocortical stimulation (ECS) mapping to localize language areas, and the Wechsler Memory Scale-Revised (WMS-R) to assess the patient’s memory. Using the findings from our functional mapping and the surgical outcome, we validated the relationship between memory function and language dominance.

2. **Patient and methods**

2.1. **Patient**

The patient was a 32-year-old left-handed female who suffered from a complex partial seizure during working time (Table 1). When the seizure occurred, she fixed her gaze at one point and turned her head toward her right, with right upper limb movement. Magnetic resonance imaging (MRI) showed no hippocampal sclerosis (Figure 1(a) and (b)), and single-photon ECT (SPECT) showed no abnormal blood flow. We examined the patient with transcranial electroencephalography (EEG) for 1 week after her admission, but no seizure was detected. Spike-like waveforms were identified on F4 during sleep, but they were insufficient for identifying the epilepsy focus. After examination, the patient was discharged and she continued taking medication. However, the epileptic seizures did not diminish and occurred more than 10 times per month. The patient had elected for epilepsy surgery; therefore, we implanted subdural grids to identify the epilepsy focus. The study was approved by the ethics committees of the Asahikawa Medich University Hospital. Written consent was obtained from the patients in accordance with the guidelines of the hospitals.

| Table 1. Demographic and clinical characteristics of the patient |
|-----------------|----------------|-------------|----------------|------------------|
| Age/Sex        | Symptoms       | Subdural grids | Epileptogenic focus | Language dominance |
| Patient        | 32/F           | Complex partial seizure | Bilateral | Left mesial temporal | Right |

![Image](https://via.placeholder.com/150)
2.2. Methods

2.2.1. Subdural grid placement and monitoring

Because the seizure focus was not detected with transcranial EEG, we implanted subdural grids over both hemispheres in regions that included the temporal base. Each ECoG grid included 70 electrodes (2 were used as a reference and a ground) spaced at 1-cm inter-electrode intervals, with each electrode having a 4-mm diameter and a 2.3-mm exposed area (Unique medical, Japan). The layout drawing was created with AVIZO (Maxnet, Japan) by combining MRI brain surface images and CT electrode data (Figure 2). After the subdural grids were implanted, the patient was monitored with Neurofax (Nihonkoden, Japan) to detect epileptic seizures. The data were sampled at 1,000 Hz with a 300-Hz high-cut filter and a 0.3-Hz low-cut filter; an AC filter also was used. The patient was monitored after the implant procedure until an epileptic seizure occurred.

2.2.2. Brain function measurements

2.2.2.1. Wada test. It was important to identify the language-dominant hemisphere before surgery because the patient was left handed. The Wada test is the gold standard technique for determining the language dominant hemisphere. We performed the Wada test in the angiography room, where we injected diluted propofol into the internal carotid arteries. The first injection was on the right side, and the second was on the left. Following the injection, the patient performed several language tasks. If the patient became aphasic after an injection, then the injected side was considered the language-dominant hemisphere. Thus, contralateral injection should not affect language function.

2.2.2.2. High gamma activity (HGA) mapping. During the ECoG recordings, the patient received visual stimuli that were presented with a monitor positioned in front of her. The patient was first asked to relax during a 20-s rest period (baseline) and then to perform the task during a subsequent 20-s period. The task consisted of hand movements, mouth movements, reading words, and naming pictures.
The ECoG data were digitally recorded at a 1,200-Hz sampling rate using a 256-channel g.HIamp amplifier (Guger Technologies, OG). The ECoG data were analyzed with CortiQ software in g.Hiamp (Prueckl et al., 2013). CortiQ performed a common average reference (CAR) to suppress common mode signals and also calculated the baseline ECoG activity for each channel in the gamma frequency range of 60–120 Hz. A t-test was used to determine whether HGA values in the active phases were significantly different from those in the baseline. p-values of <0.05 were considered statistically significant. Finally, the results were visualized in real time as a red circle presented on a monitor.

2.2.2.3. ECS mapping. ECS mapping was performed after ECoG mapping to confirm whether HGA mapping was consistent with the gold standard mapping. Electrical stimuli were delivered using Neuromaster (Nihonkoden, Japan) and with two electrodes positioned at a short inter-electrode distance. The electrical stimuli were bipolar square-wave pulses, each with a 200-μs duration, delivered at 50 Hz over a 1-ms duration at 4–8 mA. When hand or mouth movements were evoked during stimulation, we...
considered the stimulation site was located in the hand or mouth motor representation, respectively. For language mapping, we presented 3 pictures or words to the patient. The first picture or word was used as a reference. After the first presentation, we performed ECS to determine whether the patient could correctly identify the second and third pictures or words during ECS. The stimulation sites at which speech arrest or difficulties were evoked were marked as language areas. In the present study, we attempted to identify memory functional areas using ECS. Before stimulation, the patient was asked to memorize 3 out of 20 randomly presented pictures. We then delivered ECS using the same parameters used in the language tasks and asked the patient to recall the memorized pictures. When the patient could not recall at least 1 picture, we regarded that area as a memory functional area.

2.2.2.4. Memory test. Memory function was tested before and after surgery using the WMS-R.

3. Results

One epileptic seizure occurred during the monitoring period. According to the ECoG recordings, the seizure focus was located in the left mesial temporal lobe surrounding the left hippocampus (Figure 2). During the Wada test, we observed no aphasia after left side injection, but we observed total aphasia after right side injection. HGA and ECS mapping also revealed language-related activity in the right precentral gyrus (Figures 3(b) and 4). From these results, we determined the patient to have right hemisphere language dominance. Although left frontal activity appeared to be related to language, HGA mapping of mouth movement showed similar activation in the left frontal lobe, which suggested motor-related activity. HGA mapping also revealed a hand motor representation above the mouth motor representation (Figure 3(b)). The results of HGA mapping were compared with those of ECS mapping by calculating the sensitivity and specificity. For motor mapping, the sensitivity was 100% and specificity was 84%, whereas for language mapping, the sensitivity was 78% and the specificity was 73%. In addition, we identified memory functional areas using ECS. When the stimuli were delivered through electrodes positioned over the right temporal base, the patient forgot the memorized pictures (Figure 4). This phenomenon lasted for 2 min, but then naturally subsided. Stimulation applied at other areas failed to evoke memory dysfunction. We assumed that language and memory functions could be preserved if the left hippocampus was resected because functional mapping indicated that language and memory functional areas were both located in the right hemisphere.

Figure 4. Speech was influenced by ECS only for the right precentral gyrus (Red). Finger movement was evoked from the motor areas (Purple). ECS evoked seizures when the facial area was stimulated (Yellow). Memory dysfunction was induced when the right temporal base was stimulated (Blue).
We subsequently performed surgery in which we resected the entire left hippocampus, amygdala, and a part of the lateral temporal lobe (Figure 1(c) and (d)). During surgery, we monitored ECoG activity recorded with subdural grids and confirmed that no epileptogenic activity was present after resection. The patient’s post-surgical condition was good without neurological dysfunction. As the condition improved, the WMS-R was again used to examine the patient’s memory. All scores (verbal memory, visual memory, and ordinary memory) were higher than those recorded before surgery (Table 2). No seizure occurred after surgery and the patient was discharged from the hospital.

4. Discussion
In this study, a left-sided hippocampectomy was performed in a patient with epilepsy and right hemisphere language dominance. It was observed that the procedure did not cause any memory dysfunction. Thus, the present findings indicate that memory function is mainly related to the language-dominant hemisphere. In addition, we performed multimodality functional mapping, including the Wada test, HGA mapping, ECS mapping, and WMS-R. These measurements helped detect brain function and preserve memory function. Detailed presurgical functional mapping should be necessary in patients with epilepsy.

In the present case, the patient was left handed and showed right hemisphere language dominance. Statistical studies suggest that 70–90% of the world population is right handed, whereas approximately 10% is left handed (Ardila, Rosselli, de Estudios, & de Neuroepidemiologicos, 2001; Dane & Gümüstekin, 2002). Other types of handedness included mixed handedness and ambidexterity (Holder & Kateeba, 2004). In left-handed people, the incidence of right hemisphere language dominance has been reported as 15% (Rasmussen & Milner, 1977) and 27% (Knecht, Drager, et al., 2000). In those reports, only few epilepsy cases demonstrated right hemisphere language dominance with left mesial temporal epilepsy.

The left hippocampus is believed to play an important role in verbal memory (Novelly et al., 1984). The other study reported memory mapping using ECS for six left language dominant subject and showed left hippocampal ECS impaired verbal memory (Coleshill et al., 2004). However, in our case, right hippocampal ECS impaired verbal memory and no memory dysfunction occurred after left hippocampectomy. For now, the laterality of memory function was not disclosed, but this result suggests that laterality of memory function is not determined by anatomical laterality but language dominance. Of course, non-dominant side was less important for verbal memory function than dominant hemisphere, but this side thought to play a role in visual memory (Cutting, 1978; Stepankova, Fenton, Pastalkova, Kalina, & Bohbot, 2004). In this case, however, visual memory was not affected even though the left hippocampus (non-dominant side) was totally resected. Other reports have indicated that no visual memory dysfunction occurred following non-dominant side hippocampectomy (Hamberger, Seidel, McKhann, & Goodman, 2010). These findings support our present results. The post-surgical WMS-R showed improvement in all memory scores (verbal, visual, and general). The same outcome was reported in a previous study, which was due to the extinction of abnormal waveforms recorded from the contralateral hippocampus (Patrikelis et al., 2013).

Regarding functional mapping, it has been suggested that the Wada test and ECS should be replaced because of their invasiveness (Papanicolaou et al., 2014). The Wada test has a risk of vascular complication (1.3–11%) and the anesthetics used in the procedure may cause somnolence, agitation,

| Table 2. Pre- and post-operative WMS-R scores |
|---------------------------------------------|
|                              | Verbal memory | Visual memory | General memory |
| Pre-operative scores          | 54            | 87            | 57             |
| Post-operative scores         | 76            | 94            | 77             |
| Average scores                | 100.36        | 101.12        | 100.54         |
| Standard deviation            | 14.70         | 13.00         | 14.36          |
and confusion (Bauer, Reitsma, Houweling, Ferrier, & Ramsey, 2014). On the other hand, ECS has a risk of seizure and is a time-consuming procedure (Ojemann, Ojemann, Lettich, & Berger, 2008; Pouratian, Cannestra, Bookheimer, Martin, & Toga, 2004). In this study, we performed functional brain mapping with real-time HGA mapping and confirmed consistency among HGA and ECS mapping and the results of the Wada test. The usefulness of HGA mapping, including real-time mapping, has been widely reported (Hill et al., 2012; Ogawa et al., 2014; Qian et al., 2013; Roland, Brunner, Johnston, Schalk, & Leuthardt, 2010). The biggest advantage of HGA mapping is that it has low invasiveness. Although subdural grid implantation is invasive, subdural grids are necessary for epilepsy diagnosis (Bekelis et al., 2012). In terms of functional mapping, HGA mapping is a much safer technique than the Wada test and ECS mapping because it requires only spontaneous brain activity. Therefore, HGA mapping is a useful technique and has the potential to be an alternative to ECS mapping and the Wada test.

Although ECS alone was used for memory mapping, HGA mapping also could be used for memory mapping. A recent report described HGA mapping with recall activity (Kunii, Kawai, Kamada, Ota, & Saito, 2014). According to this report, memory-related HGA also showed a dominance that was similar to that for language, but the two did not always correspond. The report concluded that memory-related HGA dominance plays a more important role in memory function than language dominance. In future studies, we will develop tasks that examine memory function and that can realize real-time memory functional mapping using HGA. Our next challenge is to map language dominance and memory functional areas using HGA.

5. Conclusion

This study indicates that memory function has a strong connection to language dominance. Determining language dominance before performing hippocampectomy is useful for determining whether the resection will affect the patient’s memory. Although memory functional mapping procedure has not been established, ECS mapping allowed us to detect the site. In the future, we plan to establish HGA real-time memory mapping with visualization.

Ethical standard
This study was approved by the Ethics Committee of Asahikawa Medical University.

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Competing Interests
The authors declare no competing interest.

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