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Recollection of vivid memories after perirhinal region stimulations: synchronization in the theta range of spatially distributed brain areas

Emmanuel Barbeau^{a,*}, Fabrice Wendling^b, Jean Régis^a, Roderick Duncan^c, Michel Poncet^a,
Patrick Chauvel^a, Fabrice Bartolomei^a

^a Laboratoire de Neurophysiologie et de Neuropsychologie, INSERM EMI-U 9926, Faculté de Médecine, 27 Boulevard Jean Moulin, 13385 Marseille, France

^b Laboratoire Traitement du Signal et de l'Image, INSERM EPI 9934, Université de Rennes 1, Campus de Beaulieu, 35042 Rennes Cedex, France

^c Department of Neurology, Institute of Neurological Sciences, Glasgow G51 4TF, Scotland

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Abstract

Electrical stimulation of the temporal cortex in patients with epilepsy sometimes elicits experiential phenomena such as recollection of vivid memories. The neurophysiological substrate of such phenomena is poorly understood. Furthermore, the relation between the site of stimulation and the type of memory elicited has only recently started to be investigated. We investigated these issues in patient FGA who had intracerebral electrodes stereotaxically implanted in the right temporal lobe for investigation of drug-resistant epilepsy. We report the results of electrical stimulations of the perirhinal region. Two stimulations elicited experiential phenomena consisting of visual memories that belonged to FGA's past, but which were not related to any particular episode. These visual memories consisted of objects or of details of objects. These two stimulations were contrasted with other stimulations in the same subhippocampal region. Cross-correlation analysis of the depth-EEG signals filtered in frequency sub-bands revealed that experiential phenomena occurred only when the various brain structures involved in the after-discharge were synchronized in the theta range. These structures included the perirhinal region, the hippocampus, other limbic structures as well as a primary visual area. Our results suggest that recollection of vivid memory after electric stimulation of the cortex may rely on wide networks of brain areas that transiently synchronize. These results also highlight the role of the perirhinal region in human memory. Experiential phenomena are rarely obtained after brain stimulation. Replication of these results is thus required due to the small number of observations reported.

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Keywords: Experiential phenomena; Synchronization measure; Cortical networks; Visual memory

1. Introduction

Electrical stimulation of the temporal cortex may elicit experiential phenomena, such as recollection of vivid memories or feelings of familiarity (“*déjà-vu*”/“*déjà vécu*”) (Bancaud, Brunet-Bourgin, Chauvel, & Halgren, 1994; Penfield & Perrot, 1963). Unlike stimulation of primary sensory or motor cortices, the results of which tend to remain constant across

patients and specific anatomical areas, the results of stimulation of temporal lobes may vary. Within the same patient, a specific experiential phenomenon can be elicited by stimulation at a given site on one occasion but may or may not be at another (Bancaud et al., 1994; Halgren, Walter, Cherlow, & Crandall, 1978). This has made it difficult to identify the mechanisms underlying experiential phenomena and different theories have been proposed within this frame.

Jackson viewed experiential phenomena as being the result of a release mechanism: spontaneous seizures would prevent a higher level centre (e.g. the limbic system) from exerting its normal control on other centres, thus allowing old memories to come to consciousness, resulting in a “dreamy state” (Jackson & Colman, 1898). On the other hand, Penfield

* Corresponding author. Present address: Service de Neurologie et de Neuropsychologie du Pr Poncet, CHU Timone 6^{ème} étage, 264, rue Saint-Pierre, 13385 Marseille Cedex 05, France. Tel.: +33 4 91 38 59 28; fax: +33 4 91 38 49 22.

E-mail address: emmanuel.barbeau@medecine.univ-mrs.fr (E. Barbeau).

considered that stimulations were reactivating stored memory traces, experiential phenomena being viewed as replays of engrams, like a “tape-recording” (Penfield, 1952). A general theoretical framework to account for these effects was provided by Gloor (1990). He suggested that electrical stimulation could induce the elaboration of patterns of excitation and inhibition in widely distributed neural networks, some of which might be capable of representing the substrate of a given previous experience in a caricatured way.

The importance of medial temporal lobe structures for experiential phenomena was recognized very early by the pioneering work of Jackson (Jackson & Colman, 1898; Jackson & Stewart, 1899). However, Penfield and Perrot (1963) induced experiential phenomena through stimulation of temporal neocortex in a considerable number of patients. They suggested that there were bidirectional connections between temporal cortices (where traces would be stored) and a “centrencephalic system” serving to integrate the trace (Penfield & Jasper, 1954). One of the latest studies on the subject reconciled these views, finding that experiential phenomena depended upon neural networks engaging both medial and lateral aspects of the temporal lobes, with the anterior hippocampus, amygdala and superior temporal gyrus having privileged access to this circuit (Bancaud et al., 1994).

Current ideas about the mechanisms subtending experiential phenomena, and our understanding of brain structures involved in such phenomena, converge on the notion that experiential phenomena depend on the activation of distributed neural networks. These networks are thought to rely on different neural assemblies scattered in different association cortices and limbic areas that embed different aspects of a specific experience (Bancaud et al., 1994; Halgren & Chauvel, 1993; see also Mesulam, 1990). Within the domain of experiential phenomena, these neural networks have to our knowledge never been formally demonstrated and physiological mechanisms subtending them are unknown.

A second issue related to memory phenomena elicited in epileptic patients is that authors working on the subject have not previously attempted to analyze the memory phenomena according to the type of memory elicited (e.g. semantic or episodic memory). This may be due to the fact that it is only recently that attempts have been made to fractionate declarative memory into subsystems (Mishkin, Vargha-Khadem, & Gadian, 1998; Tulving & Markowitsch, 1998) and because this point is much debated (Squire & Zola, 1998). Without these putative theoretical frames in mind, and given the variability of the results after stimulation discussed above, most authors have found that experiential phenomena related to memory were idiosyncratic and strongly related to the interpersonal psychological state between the patient and the examiner (Halgren, 1984).

We recently studied the effects of electrical stimulation of medial temporal lobe structures in a series of 24 patients and demonstrated dissociable effects whether the amygdalo-hippocampal structure, the entorhinal or the perirhinal cortex were stimulated (Bartolomei et al., 2004). In the present

study, we extracted one patient from this series on the basis of him reporting particularly well-described experiential phenomena. Our objective was two-fold. First, we wanted to study whether experiential phenomena relied on transient neural networks as hypothesized above. Second, we wanted to assess whether the type of memory reported by this patient was idiosyncratic (e.g. related to personality traits) or, in contrast, was relevant to current models of memory (e.g. related to the site of stimulation).

2. Methods

2.1. Patient

FGA, a 33 years old ambidextrous male, had complex partial seizures since the age of 21. He had 14 years of successful education. He had no history of psychiatric illness. Neuropsychological assessment (Table 1) revealed normal intelligence (total IQ: 104) as well as normal memory (MQ: 108, delayed MQ: 114) both in the verbal and visual domain.

Anticonvulsant drugs failed to control the seizures, and presurgical evaluation was performed. MRI showed no signs of hippocampal sclerosis or other lesion. Volumetric measurements of hippocampal and entorhinal cortex revealed a slight diminution of right hippocampal volume (FGA: 4173 mm³, 12 control subjects: 4800, S.D. = 324, Z-score = -1.93) and normal right entorhinal cortex volume (FGA: 1434 mm³, control subjects: 1635, S.D. = 181, Z-score = -1.11). Video-EEG recordings of seizures consistently suggested right temporal lobe epilepsy, with a posterior temporal (maximal over T4-O2 bipolar recording) theta discharge. The seizures started with a sensation of ascending epigastric tightness, anxiety, and nausea and were followed by loss of consciousness with staring and unresponsiveness. The absence of clear signs of hippocampal sclerosis and the posterior predominance of the ictal discharge led to the decision to carry out invasive recording.

Stereoelectroencephalographic (SEEG) recording was performed in order to precisely define the epileptogenic zone, in particular the respective involvement of the medial and lateral structures and the posterior limit of the epileptogenic

Table 1
FGA neuropsychological assessment

WAIS-III	
Verbal IQ	107
Performance IQ	98
Total IQ	103
WMS-R	
Verbal MQ	106
Visual MQ	102
General MQ	108
Attention	115
Delayed MQ	114

All measures: mean = 100, S.D. = 15. WAIS-III: Wechsler Adult Intelligence Scale-III; WMS-R: Wechsler Memory Scale-Revised.

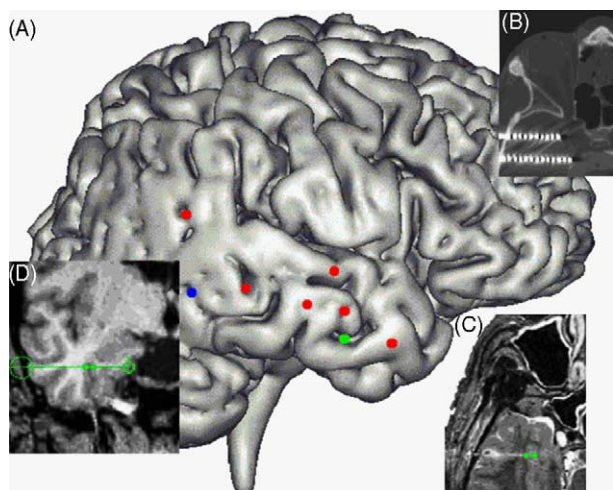


Fig. 1. (A) Three-dimensional surface reconstruction of the right hemisphere of FGA, with the site of implantation of each electrode. In green is shown the implantation site of the electrode running through the perirhinal region. In blue is shown the electrode whose medial part runs into the primary visual cortex (see text for details). (B) A CT-scan showing contact location. (C) Post-SEEG axial MRI showing the thin trace left by the electrode. (D) Coronal MRI showing the stimulation site (green dots) in the depth of the occipito-temporal sulcus of the right temporal lobe, an area that corresponds to the perirhinal region (see text for discussion).

zone. FGA was fully informed about the aim of the investigation before giving his consent. He had eight intracerebral electrodes implanted stereotaxically in the right temporal lobe orthogonal to the midline vertical plane (Fig. 1A). Each electrode was from 33.5 to 51 mm long, had a diameter of 0.8 mm and contained from 10 to 15 contacts 2 mm long separated by 1.5 mm (Dixi Medical, France). A total of 110 intracerebral contacts were simultaneously recorded. The sampling frequency of EEG depth-recording was 256 Hz with an analogue filter band-pass of 1–100 Hz (Deltamed, France).

SEEG revealed that spontaneous seizures began with an epileptiform discharge affecting the right anterior part of the hippocampus and the amygdala, which secondarily involved the posterior part of the hippocampus, the anterior subhippocampal gyrus and the temporal neocortex. Anterior temporal lobectomy was performed and the patient is currently seizure free after 18-month follow-up.

2.2. The location of the electrode contacts

Each electrode was inserted stereotaxically under general anesthesia. A postoperative CT-scan without contrast was performed to check for the absence of bleeding and for the precise location of each contact (Fig. 1B). MRI with 3D reconstruction was performed the day after removal of electrodes in order to locate the trace of each electrode in the brain (Fig. 1C). The fusion of the postoperative CT-scan with this MRI allowed precise anatomical localization of contacts: the distance from the mid-line vertical plane of a given contact

could be calculated on the axial CT-scan. After the trace of the electrode had been found on the postoperative axial MRI, the distance from the mid-line vertical plane could be reported and the reported position of the contact could then also be viewed in the coronal or sagittal plane (Fig. 1D). After this procedure was completed, the anatomic structures in which contacts were located were identified using 3D verification.

2.3. Electrical stimulations

Electrical stimulations were applied to each contact in the grey matter as part of the standard functional and epileptogenic mapping procedure to delineate surgical resection. Square wave pulses of alternating polarity were generated in 5 s trains (1 ms duration, 50 pulses/s). All stimulations were bipolar between two adjacent contacts.

2.4. Analysis of functional coupling

Synchronization measures between EEG signals recorded from different brain regions can be used to characterize functional networks involved in specific cognitive functions. The basic idea is to estimate a statistical relationship between signals and to interpret results in terms of functional coupling between neural assemblies that generate analyzed signals.

In the present work, cross-correlation was used to determine whether samples contained in a temporal sliding window defined on two depth-EEG signals from two separate channels are correlated (Fig. 2A and B). The method is applied on a bandpass filtered version of depth-EEG signals to evaluate their linear relationship as a function of both time and frequency band (Wendling, Bartolomei, Bellanger, Bourien, & Chauvel, 2003). The procedure consists of three steps. Firstly, the two signals to be analyzed are filtered using a filter bank whose cut-off frequencies were chosen in accordance with classical EEG frequency sub-bands (Fig. 2C). Secondly, a first quantity referred to as the linear correlation coefficient r^2 is estimated on each pair of filtered signals X and Y as a function of time (Fig. 2D). r^2 -values range from 0.0 to +1.0. Thirdly, a second quantity, referred to as the time delay τ_{XY} and conjointly computed with coefficient r^2 on each pair of filtered signals is represented as a function of time on a specific frequency band (Fig. 2E). For significantly high r^2 -values, τ_{XY} gives insight into the latency relationship between oscillations of signals X and Y . τ_{XY} -values are expressed in milliseconds. If the signal from one structure is constantly delayed with respect to the signal from the second structure, it can be argued that there exists a causal relationship and, by extension, that the activity generated by the first structure may be led by that from the second one (Pijn & Lopes Da Silva, 1993).

2.5. Statistical analysis

r^2 - and τ_{XY} -values between pairs of signals recorded during the after-discharge were computed before and after elec-

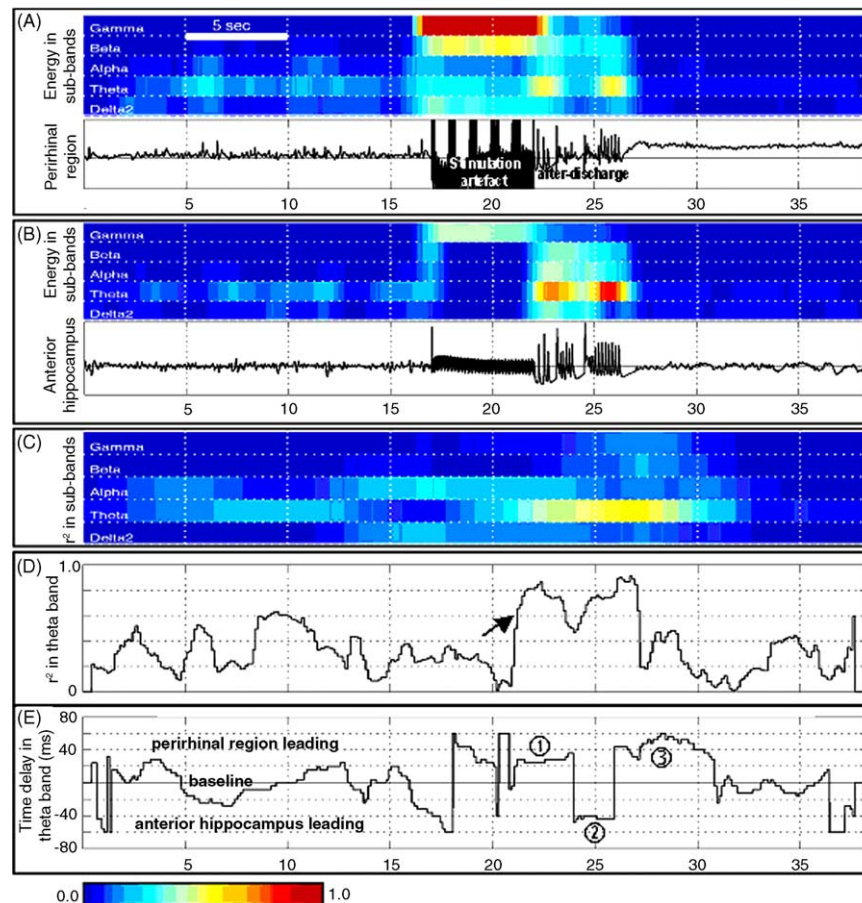


Fig. 2. (A) Bottom: depth-EEG signal recorded from the perirhinal region before ($t < 17$ s), during ($17 \text{ s} < t < 22$ s) and after ($t > 22$ s) electrical stimulation. An after-discharge ($22 \text{ s} < t < 27$ s) is observed after the stimulation artefact. Top: distribution of the normalized average energy in frequency bands. During the stimulation, the energy is mainly distributed on the gamma band since the stimulation frequency is 50 Hz. Theta activity is predominant during the after-discharge. (B) The signal recorded over the same period from the anterior hippocampus with corresponding energy distribution. An after-discharge is observed whose energy mainly concentrates in the theta band. (C) Distribution of normalized average energy in frequency bands from both perirhinal region and anterior hippocampus. Most energy concentrates in the theta band during the after-discharge. (D) Evolution of r^2 -values in the theta band as a function of time. r^2 -values rise during the after-discharge (arrow). (E) Evolution of time delay τ_{XY} between signals recorded from the perirhinal region and anterior hippocampus as a function of time. During the after-discharge, τ_{XY} -values in the theta band show a complex interaction between the perirhinal region and anterior hippocampus (see ①, ②, ③).

trical stimulation for all structures that were activated during the after-discharge. Significantly high r^2 -values were determined from a statistical t -test performed on r^2 -values measured before and after electrical stimulation, after Gaussian correction (Bendat & Piersol, 1971). Relationships among cerebral structures according to r^2 and τ_{XY} analysis were synthesized in a diagram that was further constrained by anatomical connections between these structures.

3. Results

We report the results of four stimulations of the contacts of an electrode running through the anterior and basal portion of the right temporal lobe (Fig. 1A): an initial stimulation applied between contacts 5–6 at 2 mA, two stimulations at contacts 4–5 at 2 then at 2.5 mA and then a fourth stimulation at contacts 1–2 at 1.5 mA. Contact 1 is the most medial

while contact 5 is the most lateral. The four stimulations reported here were all successively applied within about half an hour by the same examiner, while the patient remained comfortably reclined on his bed. He had no way of knowing when stimulations were applied, and was instructed to read aloud and report anything unusual he would notice.

Stimulations through contacts 4–5 (stimulations 2 and 3) evoked experiential phenomena consisting of vivid memories in our patient. No other stimulation evoked any experience with memory-like content although the anterior and posterior hippocampus, the amygdala and the parahippocampal cortex were also stimulated. Contacts 4–5 were located just lateral to the perirhinal cortex (Insausti et al., 1998; Suzuki & Amaral, 1994) (Fig. 1C), an area known in the monkey as area TE or Brodmann area 20. Recent work on the perirhinal cortex in the monkey suggests that it may extend farther laterally than has been thought until now (Suzuki & Amaral, 2003). Area TE projects massively to the perirhinal cortex (Suzuki &

Amaral, 2004) and neurons with similar properties have been found in both structures (Xiang & Brown, 1998). Both areas are anterior subhippocampal structures functionally related as they belong to the visual ventral stream. The area where contacts 4–5 are located will henceforth be referred to as “the perirhinal region” for the sake of simplicity.

3.1. Stimulation 1: Contacts 5–6 at 2 mA

Electrical stimulation through contacts 5–6 at 2 mA yielded a small after-discharge 5 s long (Fig. 3) visible in the anterior and posterior hippocampus, the entorhinal cortex and the perirhinal region, the amygdala and, with a slight delay, in a visual area located in a posterior and medial branch of the collateral sulcus (stimulation of this visual area elicited elementary hallucinations such as twinkling round shapes in the left visual field). The patient did not report feeling or seeing anything during stimulation or during the after-discharge.

Functional coupling analysis of the results of this stimulation revealed two networks: one centred on the perirhinal region in the theta range (3.5–7.4 Hz) and another centred on the anterior hippocampus in the alpha range (7.5–12.4 Hz) (Fig. 4A and B). There was no indication of functional coupling between either region and the aforementioned visual area.

3.2. Stimulation 2: Contacts 4–5 at 2 mA

Stimulation through these contacts yielded a small after-discharge of the same duration involving the same structures as the previous stimulation. The after-discharge was however of a different pattern, with slower rhythm in the anterior hip-

pocampus (Fig. 5, ①) and earlier involvement of the visual cortex (Fig. 5, ②), as can be compared with Fig. 3.

Immediately on stimulation, the patient said an image was coming but that it was hard to see, as it was too faint. He then said he had seen a lake, which was behind his house. He added: “I go there very often”. Upon later questioning, he was able to explain that he had only seen the lake and then, a while after, some bushes.

Functional coupling analysis revealed a different network of activation between medial temporal lobe structures (Fig. 4C), as energy was maximum in the theta range. All r^2 -values between structures depicted in Fig. 4C were significantly different from those measured between these same structures at rest (Fig. 4C versus Fig. 4A, $p < 0.001$). Furthermore, contrary to the previous stimulation, a strong relation in the theta range was found between the anterior hippocampus and the perirhinal region with the visual area. Analysis of time delay τ_{XY} indicated that the leading signal shifted one or several times between structures during the after-discharge. Specifically, the signal from the anterior hippocampus first led that from the perirhinal region, and then the situation reversed.

3.3. Stimulation 3: Contacts 4–5 at 2.5 mA

A second stimulation at 2.5 mA, a slightly higher intensity than the previous one, was applied through the same contacts. The subsequent after-discharge had exactly the same pattern as the previous one (not shown). The patient immediately said that something had materialized and that it was a neighbor going by in the street on a motorbike. He added: “I see him very often” and said that it was his brother’s friend. Ques-

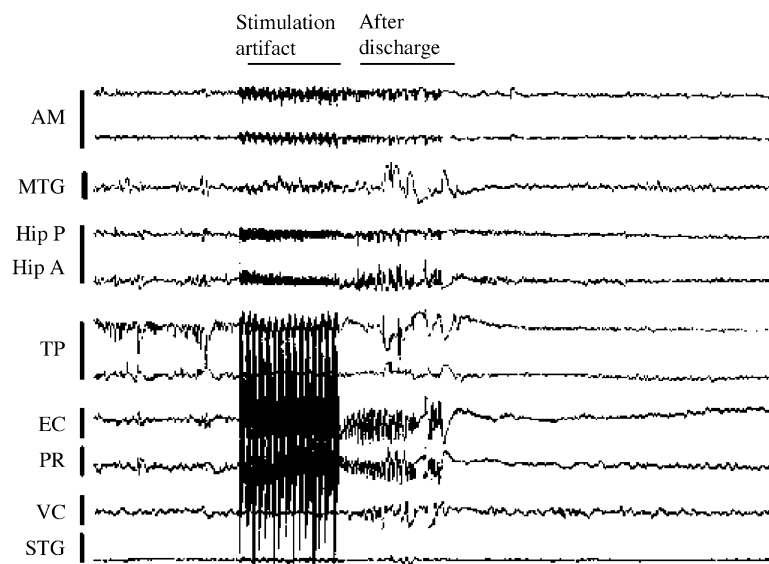


Fig. 3. Summary of the SEEG traces during stimulation of contacts 5–6 at 2 mA. This stimulation induced an after-discharge that predominated in the amygdala, the hippocampus and the rhinal region. Note the slight and delayed modification in the visual region. *Abbreviations*—AM: amygdala, MTG: middle temporal gyrus, Hip P: posterior hippocampus, Hip A: anterior hippocampus, TP: temporal pole, EC: entorhinal cortex, PR: perirhinal region, VC: visual cortex, STG: superior temporal gyrus.

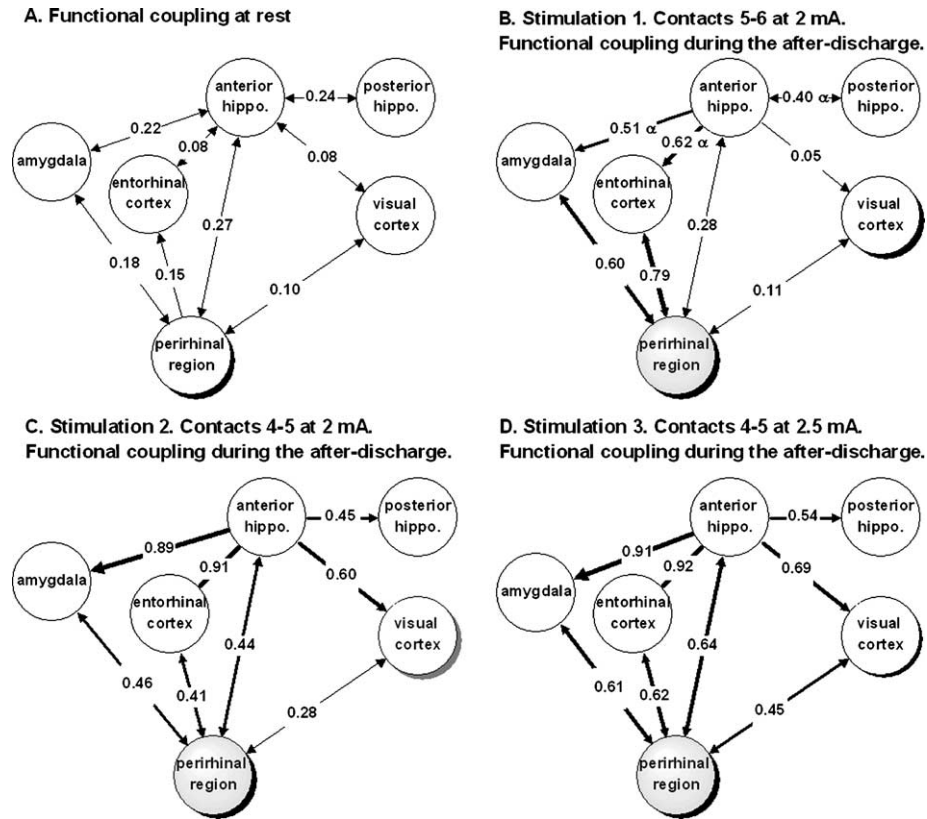


Fig. 4. Functional coupling between the anatomical structures involved in the after-discharge showing the correlation coefficient r^2 . All analyses were conducted in the frequency range where most energy was observed: in the theta range in A, C and D unless mentioned otherwise in B (α = alpha range otherwise theta range). The arrows indicate which structure is being driven according to time delay τ_{XY} . Double arrows indicate that two structures alternately take the lead. A line indicates that time delay τ_{XY} between two structures is below 10 ms. The thickness of the arrows is related to the value of r^2 . Anterior hippo.: anterior hippocampus, posterior hippo.: posterior hippocampus. (A) Functional coupling at rest (analyzed here in the theta range). (B) Functional coupling following stimulation of contacts 5–6 at 2 mA. (C) Functional coupling during the after-discharge following stimulation of contacts 4–5 at 2 mA. (D) Functional coupling following stimulation of contacts 4–5 at 2.5 mA.

tioned later, he explained that he had seen a chromed part of a motor, then a black-leathered boot and that he had inferred from these “distinct signs” that the person he was seeing was his brother’s friend.

The patient was not able to relate this memory or the previous one (stimulation 2) to any specific past event and insisted that it was quite usual for him to go to the lake or to see his brother’s friend with his motorbike. Both memories were vi-

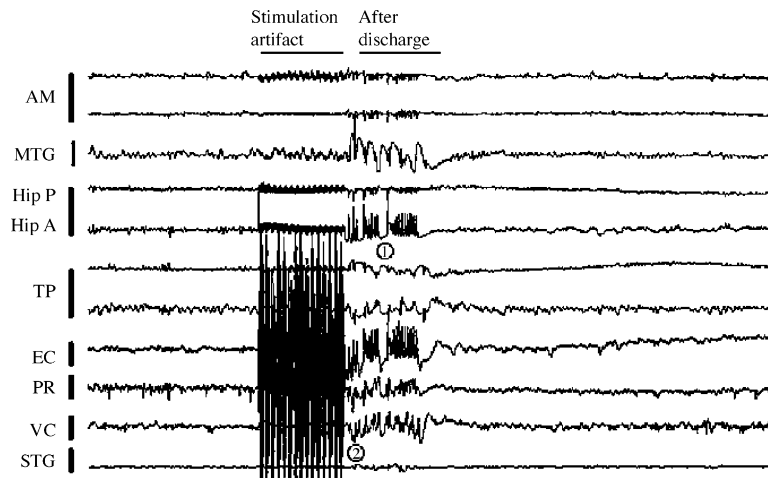


Fig. 5. Summary of the SEEG traces during stimulation of contacts 4–5 at 2 mA. This stimulation induced an after-discharge with a synchronous appearance in the amygdala, the hippocampus, the rhinal region and the visual region. For abbreviations, see Fig. 3. ① and ② see text.

sual, coloured, with no movement, feeling or emotion. FGA was completely aware of his hallucinations. He remembered them well afterwards and was able to specify that he really had the sensation of “seeing” the objects first and that it was a moment after that he was able to relate them to a complete memory.

Functional coupling analysis revealed a network of activation similar to that seen after the 2 mA stimulation of contacts 4–5 (Fig. 4D). An example of how r^2 between the hippocampus and the perirhinal region varied after this stimulation is provided in Fig. 2D (top). τ_{XY} Shifts between the perirhinal region and anterior hippocampus during the after-discharge were also observed (Fig. 2D, bottom).

3.4. Stimulation 4: Contacts 1–2 at 1.5 mA

Stimulation of these contacts, which were located in the entorhinal cortex, yielded a long after-discharge, which lasted about 60 s and involved all sampled medial temporal lobe structures including the perirhinal region, but not the visual area. The patient did not report seeing anything, but did report anxiety and epigastric tightness, symptoms very similar to the prodrome of his spontaneous seizures.

4. Discussion

In our patient, two electrical stimulations of the perirhinal region elicited experiential phenomena related to memory. Those memories were visual and consisted of objects or of details of objects. They were related to semantic autobiographical knowledge (Kopelman, Wilson, & Baddeley, 1990). Our patient each time spontaneously stated that he had “often” seen the objects. Those were not related to any particular single episode, but still were related to his own personal experiences.

Functional coupling analysis of after-discharges during those two stimulations revealed high correlation in the theta range among signals recorded in MTL structures, and between MTL structures and a primary visual area. Another stimulation (the first) induced a similar after-discharge in the same structures, but no experiential phenomenon was elicited. Functional coupling analysis showed that the perirhinal region and the anterior hippocampus were not synchronized in the same frequency range, and that the level of coupling between these structures and the visual area was not different from normal activity at rest. Synchrony in the theta range between these three structures thus seemed to be required to enable experiential phenomena in our patient. This interpretation is further supported by the last stimulation. The stimulation of the same electrode more medially started an after-discharge in all MTL structures but not in the visual cortex. No experiential phenomenon was induced, suggesting that activation of MTL structures alone was not sufficient to evoke experiential phenomena in this patient.

This analysis is well supported by the pattern of the after-discharges elicited by the stimulations. The visual primary cortex was involved with a slight delay and rhythms were faster in the hippocampus during the after-discharge elicited by the first stimulation, as can be seen in Fig. 3. In contrast, the visual primary cortex was involved simultaneously and rhythms were slower in the hippocampus during the second after-discharge that elicited vivid recollection, as can be observed in Fig. 5. These after-discharges, although very similar, thus show slight differences that are in line with the notion that vivid recollection in this patient was supported by simultaneous synchronization in the same rhythms of spatially distributed brain areas.

A third line of evidence supports the notion that wide neural networks may have transiently formed that supported vivid recollection in our patient. The nature of the memory that was elicited is indeed in good accordance with the theoretical functional contribution of the different brain areas involved in the neural networks that were revealed by functional analysis. For example, the primary visual area was synchronized with the hippocampus and the perirhinal region and may have supported the visual characteristics of the patient’s experience. It has been shown that sensory-specific neural areas are reactivated during sensory-specific information retrieval (Kosslyn, Ganis, & Thompson, 2001; Wheeler, Petersen, & Buckner, 2001). It is worth mentioning that other visual areas higher up in the visual pathway also probably participated to the experiential phenomena but were not recorded with the available electrodes.

A characteristic of the memory elicited in our patient was that it was visual memory that belonged to his past. The perirhinal region has been implicated in visual recognition memory (both short- and long-term) in animals and humans (Aggleton & Shaw, 1996; Buffalo et al., 1999; Meunier, Bachevalier, Mishkin, & Murray, 1993). Our patient saw only single objects or details of objects. This is in accord with suggestions linking the perirhinal region to the visual ventral stream and to its relative specialization in memory for unique items (Murray & Richmond, 2001). In addition, the memory elicited in our patient belonged more to context-free, often experienced, semantic memory than to context-dependant, uniquely experienced, episodic memory. Semantic memory is thought to largely depend on the ventral stream and on anterior subhippocampal structures (Tulving & Markowitsch, 1998; Vargha-Khadem et al., 1997). Memories reported by our patient were over-learned, which may explain why he was able to recall them rather than just have a sense of familiarity with them (Aggleton & Brown, 1999; Norman & O’Reilly, 2003).

In summary, we interpret our data in the following manner: different local areas cooperated to form a transient global network (Bressler & Kelso, 2001), each making its own functional contribution to the cognitive process. These areas, which included the visual cortex, the perirhinal region and the hippocampus as well as others whose contribution was not analyzed here, were able to work in concert using the

mechanism of synchronization. This transient network was not static, as signal latency analysis revealed complex interactions between the perirhinal region and the anterior hippocampus, two areas that seemed crucial for the experiential phenomena elicited in our patient. Each led the other in alternating fashion, suggesting a dynamic network rather than a purely bottom-up or top-down exchange of information. It is noteworthy that this dynamic network was not generated at random but seemed to be functionally strongly related to the initial site of stimulation. Here, the perirhinal region was stimulated and the patient reported semantic-like experiential phenomena consisting of objects or of details of objects. Other authors have reported purely episodic autobiographical memory experiential phenomena after stimulations of the amygdala or the hippocampus. For example, Patient 3 of Gloor, Olivier, Quesney, Andermann, and Horowitz (1982) reported after stimulation of the hippocampus: “*I have a feeling of people coming back. It is this Indian guy who was here yesterday*”. In this case, the patient spontaneously reports the what, where and when of the episode (see also Patient 5, Bartolomei et al., 2004; Gloor et al., 1982), which strongly contrasts with the experiences reported by our patient, who saw only objects and spontaneously used the term “often” when reporting experiential phenomena. The fact that our patient reported only objects may be attributable to the site of stimulation, located in a region that encompassed the perirhinal cortex and area TE, two areas crucial for high-level memory of objects (see contact location in Section 3).

In humans, theta synchronization has been implicated in memory recollection and recognition in several studies using scalp-EEG (Klimesch et al., 2001). Subdural recordings in epilepsy patients have revealed theta rhythms during spatial navigation in a virtual maze (Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999). Interestingly, these theta rhythms were found in widespread neocortical areas and were more frequent during recall than learning trials, as has been observed in our study. Oscillations in other frequency range, and in particular in the gamma range (>30 Hz), have been implicated in memory phenomena (Herrmann, Munk, & Engel, 2004, for a review). Interaction between theta and gamma synchronization has also been observed (Fell et al., 2003). Here, energy was maximum in the theta range and increased very little in the gamma band as can be observed for example in Fig. 2C. In addition no significant coupling was found in the gamma band.

As brain waves reflect the collective behavior of neurons, our results suggest that the different regions synchronized in the theta range built up a transient functional neural network related to the experiential phenomena. If so, then synchronization may be the physiological mechanism subtending experiential phenomena, enabling coordination of spatially distributed brain regions. Although wide neural networks have been postulated to support experiential phenomena (Bancaud et al., 1994; Gloor, 1990; Halgren & Chauvel, 1993), there had been to our knowledge no supporting evidence until now.

Stimulation was carried out in this patient as a part of a clinical evaluation, and the results were analyzed after the end of the SEEG recording, so the stimulations could not be repeated. Due to the rarity of experiential phenomena, only two such episodes were reported in this study, which raise the question of the reliability of the findings. Replication of these results is thus clearly needed. Notwithstanding, this study highlights the potential usefulness of assessing temporal characteristics of neuronal responses during experiential phenomena. It also suggests directions for future investigations and illustrates the way in which the study of experiential phenomena may be relevant to the study of memory in the human brain.

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