Model of the hippocampo-cortical connectivity in “Temporal Consciousness” in normal and pathological memory: The Hippocampus, Memory and Temporal Consciousness project

Modélisation des interactions entre l’hippocampe et le cortex dans « la Conscience Temporelle » dans le fonctionnement normal et pathologique de la mémoire: le projet Hippocampe, Mémoire et Conscience Temporelle

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Abstract

Within the framework of Memory, Consciousness and Temporality Theory (MCTT) confabulation is not a ‘pure’ memory disorder, but rather a pathological condition that involves the Temporal Consciousness (TC), (i.e. being conscious of one’s own past, present and future). According to the MCTT, TC remains unimpaired in confabulating patients, as it is in normal subject, but it does not operate correctly. There is an increasing converging evidence that lesions, which produce amnesia also produce deficits of TC. This suggests that the integrity of the medial temporal lobe (MTL) and related structures is crucial for the normal functioning of TC. The overall goal of the study is to evaluate the role of the MTL (in particular the hippocampus) and of its connections to other cortical areas in cognitive tasks related to TC. We mainly focus on the theoretical framework of the work and we describe the cognitive task that will be used to evaluate TC in normal subjects and in patients with memory disorder.

Keywords: Confabulation; Memory; Consciousness; Time; Memory Disorder

Résumé

Dans le cadre de la Memory Consciousness and Temporality Theory (MCTT), la confabulation n’est pas considérée comme un pur déficit de mémoire, mais plutôt comme une condition pathologique plus complexe, qui implique la Conscience Temporelle (CT) (i.e. être conscient de son propre passé, ainsi que de son propre présent et futur). Selon la MCTT, la CT est encore intacte chez les patients confabulateurs, comme chez les sujets sains, mais son fonctionnement est anormal. Il existe des preuves convergentes du fait que des lésions qui produisent l’amnésie produisent également un dysfonctionnement de la CT. Cela suggère que l’intégrité du lobe temporal médial (LTM) et de structures liées est cruciale pour le fonctionnement normal de la CT. L’objectif principal de cette étude est d’évaluer le rôle du LTM (en particulier de l’hippocampe) et de ses connections avec d’autres zones cérébrales dans les tâches cognitives utilisées pour l’évaluation de la CT. Nous décrivons ici le cadre théorique dans lequel ce projet s’inscrit ainsi que la tâche cognitive utilisée en vue d’évaluer la CT pour les sujets sains et pour les différentes populations pathologiques étudiées.

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Mots clés : Confabulation, Mémoire, Conscience, Temporalité, Déficit de mémoire

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1. Introduction

Memory disorders are not only characterized by forgetting. “Memory distortions” also occur, and, among these, confabulation, which consists in actions and verbal statements that are inconsistent with the patient’s history, background, present and future [1,2].

It is known that confabulation is not limited to remembering personal past episodes, but also involves the patient’s present and future [3–6].

Patients who confabulate not only remember “another” past but are also living “another” present and planning “another” future. Hence, confabulation, like amnesia, is not a pure memory phenomenon, but it concerns Temporal Consciousness (TC) that is personal temporality, past, present and future, as a whole. TC opens the possibility of a temporal existence for the subject. A subject aware of a temporal existence is conscious of a personal past when remembering, a personal present, in which he/she is oriented, and a personal future, in which he/she is projected. These ideas are part of the Memory Consciousness and Temporality Theory (MCTT), which has been detailed elsewhere [1].

In this paper we present the Hippocampus, Memory and Temporal Consciousness Project. Its principal aim is to study the functioning of TC and its neural correlates in normal subjects and in different types of memory disorders. We first describe the MCTT, that represents the main theoretical framework of this study and after a description of the principal objectives we detail the different types of population, which are planned to be studied. We then focus on describing a task concerning the cognitive and neuropsychological evaluation of TC, in particular the Confabulation Battery.

2. The Memory, Consciousness and Temporality Theory (MCTT)

The MCTT relies on a hypothesis concerning the relation between memory, consciousness and temporality in normal subjects (Fig. 1) and in confabulation (Fig. 2).

![Figure 1: A hypothesis concerning the normal relation between memory, consciousness, and temporality. NS: nervous system; X, Y: patterns of modification of the nervous system. X: less stable pattern, Y: more stable pattern. Less stable modifications of the brain are linked to the TC, which address the uniqueness of the object consciousness (unique event with a specific temporal context). More stable modifications of the brain (Y) are related to the KC, which address the multiplicity of the object consciousness (repeated events, like habits and over-learned information).](image1)

![Figure 2: Abnormal functioning of TC in confabulation (TC addresses M as U). In confabulating patients TC remains present but is not interacting with less stable patterns of modification of the brain, because these modifications are abolished or inaccessible. In this condition TC interacts with more stable patterns of modification of the brain and addresses the object’s M, habits, routines, repeated events as U a specific unique past event.](image2)

The most important aspects of the MCTT relevant to the interpretation of confabulation are summarized here:

- events produce atemporal and aspecific modifications in the brain. These modifications, represented in Fig. 1 as X, Y, are atemporal in the sense that they do not contain any information concerning time. They are aspecific in the sense that they do not contain any information specifying that they are representing episodes, meanings, rules, procedures, algorithms, etc.;
- the modifications in the brain can be more or less stable or more or less vulnerable depending on a number of variables. These variables include, attention at encoding, emotional value of the event, depth of encoding, repeated experience of the same event, etc.;
- Consciousness means to be conscious “of something in a specific way”. That means that consciousness is not an aspecific dimension that passively receives different types of already specified information and become aware of it, but rather that different types of consciousness exist, each representing an original and irreducible way of addressing the world. Different types of consciousness include, among other Temporal Consciousness and Knowing Consciousness (KC). TC means to become aware of something as part of a personal past, present or future, KC means to become aware of something as a meaning or as an element of impersonal knowledge (i.e. information not referring to specific personal episodes);
- the object of consciousness represents a determination and an undetermination, what we have called U(niqueness) and M(ultiplicity). TC addresses the object’s U, whereas KC addresses its M. For example, this pen on the desk is both “a pen” and “the pen”. In the first case it is an undetermined pen, something that belongs to the category of “pens”, an object that I recognize and use appropriately because I recognize it. On the contrary in the second case “the pen” is a determined object, it is exactly this pen in front of me, the pen I bought yesterday and that I will be using tomorrow. So the pen reveals a U and a M. M is reflected in its being a pen
and not a different object. U manifests itself in its being this precise pen and not another;
• less stable and more vulnerable patterns of modifications of the brain are necessary, but not sufficient, for the interaction between TC and the object’s U, whereas more stable and less vulnerable modifications of the brain are necessary but not sufficient, for the interaction between KC and the object’s M.

According to the MCTT, in confabulating patients, TC is present, as in normal subject, and addresses the object’s U, just as in normal subjects. These patients can still remember their past, they are present to a world and they can project themselves into a personal future.

But in doing this they make errors, sometimes really bizarre errors. What is actually happening in these patients is that TC remains present, but it is not interacting with less stable patterns of modification of the brain, because these modifications are abolished or inaccessible. Most of the time the result of this condition is that personal habits and routines are considered in a personal temporal framework.

When asked what they have done the previous day or what they are going to do the following day, confabulating patients typically answer with memories and plans that they usually have in their daily life. Although admitted to the hospital, they will say, for example, that they went out shopping the previous day and that they will be visiting some friends the following day, acts that presumably were part of their routine life. According to the MCTT, in this condition, TC interacts with more stable patterns of modification of the brain and addresses the object’s M, habits, routines, repeated events as U, a specific unique past event (Fig. 2).

In non-confabulating amnesic patients we observe a loss of TC. These patients not only do not consciously remember their past, but neither can they imagine their personal future and they are lost in a “non time”, a sort of instantaneous present.

3. Neural correlates of temporal consciousness

Now the question is “which brain structures need to be intact for the normal functioning of TC? Which one are altered in confabulation, and damaged in amnesia?”.

Based on their own data and data from the literature, Dalla Barba and Boissé concluded that the absence of confabulation in patients with hippocampal lesions distinguishes them from patients with damage in other brain areas involved in memory [7]. Gilboa and Moscovitch [8] found that only two out 79 patients with confabulation had lesions involving the medial temporal lobe (MTL). These patients had lesions in more than 20 brain regions, although the frontal lobe was preferentially affected, but almost all these patients had preserved MTL. Twenty-eight additional confabulating patients not included in Gilboa’s and Moscovitch review also had preserved MTL. According to this view, the integrity of the MTL is essential for both normal and pathological episodic memory retrieval, because it is necessary in order for an individual to be conscious of a personal past, be it real or confabulated.

However, the integrity of the MTL is essential not only for normal or distorted, as in confabulation, episodic remembering of one’s own personal past, but it is also crucial for projecting one’s own personal future, i.e. the ability, for example, to predict what one would be doing next day or how one would spend next vacations. In other words, there is evidence in favor of a role of the MTL not only in episodic remembering but also in TC i.e. conscious awareness of personal past and future [1–7]. Further evidence on the involvement of the MTL in TC comes from a recent neuroimaging study, which showed that in normal subjects the hippocampus was activated both when individuals remembered their past and when they imagined their future [9].

Thus, according to the Memory, Consciousness and Temporality Theory:
• MTL seems to be a good candidate as the neural correlate of TC. It is the neural “temporal” device by which a piece of information assumes a temporal dimension, allowing individuals to be conscious of a personal past, present and future;
• lesions to the MTL determine the loss of TC, preventing individuals to remember their personal past, be oriented in the present and project their personal future;
• if the MTL is intact but other temporo-parietal areas are damaged or disconnected from it, confabulation and other types of memory distortions are present, because the MTL receives and provides a temporal dimension to altered information from these areas;
• if the MTL is intact but the orbitofrontal cortex and basal forebrain or their projections from the MTL are damaged, the MTL is working without the control and monitoring functions of these brain structures. Confabulation and other memory distortions are produced in this condition.

4. Main objectives

The aspects of the MCTT sketched here are the starting point of this project. In particular, a number of questions need an experimental answer:

• what is the in vivo connectivity and disconnection of the MTL and its relationship to normal and pathological memory?
• what is the relationship between MTL atrophy – like in Alzheimer’s disease (AD) – and normal and pathological TC?
• within the MTL, are different structures involved in different aspects of memory and TC? In particular, what is the functional neuroanatomy of different regions within the hippocampal formation?
• may memory distortions and, in general, distortions of TC be useful for improving the diagnosis of AD?

This project has a dual objective. The first one concerns basic research and aims at evaluating the role of the MTL (in particular the hippocampus) and of its connections to other cortical areas in cognitive tasks related to TC. We will evaluate this role using an experimental protocol evaluating confabulation in normal controls and different groups of patients with memory impairments, using neuropsychological tools and multimodal
An important part of the scientific program concerns the data processing and it is separated into two parts: one concerning the anatomical and MEG information, since they are closely linked, and another one concerning the DTI analysis. The last task concerns the construction and testing of the neurocomputing model according to all the neuroimaging results which should help to select the anatomical regions included in the domain, and the results of MEG localization will allow to test the different hypotheses of the nature of connectivity between MTL and cortex, and its impairment in the different forms of pathological memory.

We focus here on the fourth task, which concerns the cognitive task that we plan to use to evaluate, at quantitative and qualitative levels, confabulation in normal controls and in the different pathological population.

Confabulations will be collected with the Confabulation Battery (CB) [2–12]. The CB involves the retrieval of various kinds of information and consists of 165 questions, 15 for each of the following domains:

- **Personal Semantic Memory** (age, date of birth, current address, number of children, etc.);
- **Episodic Memory**. Episodic, autobiographical questions;
- **Orientation in Time and Place**;
- **Linguistic Semantic Memory**. Items 16 to 30 of the WAIS vocabulary subtest were selected for a word definition task;
- **Recent General Semantic Memory**. Knowledge of facts and famous people, which have been repeatedly reported in the news during the last ten years. For example, “Who is Ben Laden?”;
- **Contemporary General Semantic Memory**. Knowledge of famous facts and famous people before 1900. For example, “What happened in Paris in May 1968?”;
- **Historical General Semantic Memory**. Knowledge of famous facts and famous people before 1900. For example, “What happened in 1789?”;
- **Semantic Plans**. Knowledge of issues and events likely to happen in the next ten years. For example, “Can you tell me what you think will be the most important medical breakthrough likely to take place in the next ten years?”;
- **Episodic Plans**. Personal events likely to happen in the future. For example, “What are you going to do tomorrow?”;
- “I don’t know” Semantic. These were questions tapping semantic knowledge and constructed so as to receive the response “I don’t know” from normal subjects. For example, “What did Marilyn Monroe’s father do?”;
- “I don’t know” Episodic. These questions tapped episodic memory and were constructed so as to receive the response “I don’t know” by normal subjects. For example, “Do you remember what you did on March 13, 1985?”.

The three subordinates dimensions of temporal consciousness, present past and future, are evaluated with questions tapping orientation in time and place, Episodic Memory and Episodic Plans respectively. Questions from the 11 domains are presented to the participants in a semi-randomized order. Responses are scored as “correct”, “wrong”, “I don’t know”, and “confabulation”. For episodic memory, responses are scored “correct” when they match information obtained from the
patient’s relatives. Correct responses are self-evident for semantic memory questions. For “I don’t know” questions, both Semantic and Episodic, an “I don’t know” response is scored as correct. Since there is no external criterion that is capable enough to define confabulation, an arbitrary decision has to be made necessarily to detect it. In order to distinguish between a wrong response and a confabulation, a clear-cut decision is adopted only for answers to questions probing orientation in time. In this case the most strict criterion is chosen: answers to questions regarding the current year, season, month, day of the month, day of the week and hour of the day are judged to be confabulations only if erring for more than 5 years, one season, 2 months, 10 days, 3 days or 4 hours, respectively. Minor distortions will be considered errors, whereas major discrepancies between the expected and the given answer will be considered confabulations, regardless of their content.

6. Discussion

The principal aim of this project is to characterize the cognitive functioning and the neural correlates of “Temporal Consciousness” in healthy subjects and its dysfunctioning in different types of memory disorders.

This project will bring important new theoretical findings on memory and its impairments, by using a dual approach based on experimental and neurocomputing modeling derived from an original cognitive theory that enlarges the previous theories on episodic memory.

In a previous study [6] we have shown that patients with different pathologies and different type and site of lesions shown, with little variance, the same pattern of confabulation. In particular, we described the performance of a group of mild AD patients and a group of Confabulating amnesics (CA) of different etiology on the Confabulation Battery.

At a quantitative level, AD patients confabulated significantly less than CA patients and can be considered “mild” confabulators.

As described above, several studies have shown that in confabulating patients, the MTL is relatively intact and the most common lesion site in confabulation is in the basal forebrain [13]. Confabulation can be considered as a dysfunction of Temporal Consciousness within the framework of MCTT. TC remains present in confabulating patients, as in normal subjects, but it does not operate normally. We could argue that AD patients are “mild confabulators” because they have a reduced TC compared to CA patients, explained by a relative atrophy in the MTL. At a qualitative level, consistent with our prediction, the main finding of the La Corte et al.’s study demonstrates that the most frequently found confabulations in patients consisted of habits confabulation (i.e. confabulations consisting of personal habits, which are considered by the patient as specific personal episodes.).

To test the anatomical hypothesis concerning the neural correlates of TC, we will perform, within the framework of this project, an anatomoclinical correlation study in which the main aim is to correlate the volume of hippocampus formation to the score obtained on the Confabulation Battery by using an automated segmentation of the hippocampus [11].

If the MTL is a neural correlate of TC, according to our hypothesis, the level of confabulation should decrease with the increase of atrophy in the MTL. Advanced and innovative signal and image processing methods will be developed in order to give an accurate estimation of hippocampus functional and anatomical properties. For this, a new anatomical model will be built, based on ultra high field MR imaging. This model will give the basic prior knowledge to derive new mathematical modeling of these structures and sophisticated MEG source localization methods, to accurately estimate the hippocampus neural activity and its coherence with the activities of cortical regions. New findings on its connectivity will also be provided using high field diffusion imaging. These methodological developments will be crucial for the analysis of memory systems and more generally all systems involving the MTL.

This project has several technical challenges related to both image acquisition and image analysis methods.

The first challenge regards ultra high field MR imaging (7T) of the medial temporal lobe. For this, the consortium holds the only French Centre, which has a 7T MR imaging device. Research included in this proposition will be centered on the development of acquisition sequences for highly resolved anatomical imaging, in order to image the inner structure of the hippocampus (grey matter subparts: hippocampal subfields, CA1-CA4, dentate gyrus and subiculum; white matter subparts: alveus and fimbria) [10]. This anatomical description will be completed by the afferent and efferent white matter pathways of the hippocampus using high field diffusion tensor imaging, which is a very novel topic and has not been used so far in the international community (main afferent pathway: perforant path; main efferent pathway: alveus to fimbria to fornix).

Another challenge is to develop a new source localization method from MEG signals that will be able to differentiate the activities of different parts of the hippocampus. For this, we will use sophisticated anatomical models based on the researches performed on the 7T MRI and build high-resolution source localization methods using new regularization techniques in the inverse problem. The neurocomputing model used for modeling episodic memory and Temporal Consciousness has not yet been applied to structures such as the hippocampus, and to cognitive memory functions. If this model fits well with our hypothesis, it will be possible to generalize it to other types of memories and memory-related impairments.

Conflict of interest statement

There are no conflict of interest and the manuscript itself has never been published either electronically or in print.

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References