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Episodic autobiographical memories over the course of time: Cognitive, neuropsychological and neuroimaging findings

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ABSTRACT

The critical attributes of episodic memory are self, autonoetic consciousness and subjectively sensed time. The aim of this paper is to present a theoretical overview of our already published researches into the nature of episodic memory over the course of time. We have developed a new method of assessing *autobiographical* memory (TEMPau task), which is specially designed to measure these specific aspects, based on the sense of re-experiencing events from across the entire lifespan. Based on our findings of cognitive, neuropsychological and neuroimaging studies, new insights into episodic autobiographical memories are presented, focusing on the effects of age of the subjects interacting with time interval in healthy subjects and lesioned patients. The multifaceted and complex nature of episodic memory is emphasized and it is suggested that mental time travel through subjective time, which allows individuals to re-experience specific past events through a feeling of self-awareness, is the last feature of autobiographical memory to become fully operational in development and the first feature to go in aging and most amnesias. Our findings highlight the critical role of frontotemporal areas in constructive autobiographical memory processes, and especially hippocampus, in re-experiencing episodic details from the recent or more distant past.

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> "Yesterday evening, as I was taking a solitary walk …; I was roused from my thoughts by the warbling of a thrush perched on the uppermost branch of a birch. At that very instant, its magic notes conjured up images of the family estate … suddenly transported back into the past, I gazed once more upon the countryside where I had so often heard the thrush's song. When I listened to it then, I was as sad as I am now." (Chateaubriand, *Mémoire d'outre tombe* [Memoirs from beyond the tomb], 1848)

1. The concept of lifelong episodic autobiographical memory

In previous centuries, philosophers and psychologists regarded memory as a power of the mind responsible for our self-identity (e.g. James, 1890; Locke, 1690). It was a unique property, as illustrated by Théodule Ribot (1881): "I have made the journey from Paris to Brest a hundred times. All these images overlap to form an unclear mass—a single, vague state, if the truth be told. Of all these journeys, only those connected to some important event, be it happy or unfortunate, appear to me as memories: only those that arouse secondary states of consciousness are situated in time." In the same vein, James (1890) emphasized that "memory requires more than mere dating of a fact in the past. It must be dated in *my* past. In other words, I must think that I directly experienced its occurrence. It must have that "warmth and intimacy" … as characterizing all experiences "appropriated" by the thinker as his own" (volume I, p. 650). This view closely parallels current conceptions of episodic memory, placing an emphasis on the subjective recollective experience and on pastness. The ambition of this paper is to present a theoretical overview into the multifaceted and complex nature of episodic memory emphasizing its temporal complexity, i.e. changes with the age of subjects, interacting with the age of memories, based on our already published researches in terms of cognitive, neuropsychological, and functional neuroimaging approaches.

According to its most recent definition, episodic memory refers to personal events recollected in the context of a particular time and place – the "what", "where" and "when" – and with some reference to oneself as a participant in the episode (Tulving, 1985, 2001, 2002). With the development of the theory of episodic memory, the essence of this memory system has shifted away from specificity and towards the phenomenal experience of remembering (Brewer, 1996; Baddeley, 2001; Gardiner, 2001; Tulving, 2001,

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2002; Wheeler, Stuss, & Tulving, 1997). As such, it encompasses perceptual, affective and spatiotemporal contextual details, and gives the rememberer the feeling that a representation is the recollection of an event belonging to his or her personal past. Although this memory system contrasts with semantic memory, its operations rely on, but go beyond, the semantic memory system. Episodic and semantic memory systems are associated with two distinct states of consciousness: autonoetic and noetic consciousness. Autonoetic consciousness, which is a *sine qua non* of episodic memory, is defined by a sense of self in time and the mental reliving of subjective experiences arising from the encoding context. Hence, based on a combination of self, autonoetic consciousness and subjectively sensed time, episodic memory makes it possible to travel mentally through subjective time, from present to past, and thus to recollect, one's own previous experiences via autonoetic consciousness. The central tenet of this theory therefore revolves around phenomenological re-experiencing and the sense of self in time. The neural bases of episodic memory and autonoetic consciousness are thought to be subserved primarily by the prefrontal cortex, but also by the medial temporal lobe (Tulving & Markowitsch, 1998; Vargha-Khadem et al., 1997). By contrast, semantic memory is associated with noetic consciousness, which denotes the subject's ability to be aware of information about the world in the absence of any remembering, and is subserved by a broad set of neocortical areas (including frontal, temporal and occipital cortices).

As episodic memory refers to events recollected in the context of a particular time and place, and with a degree of autobiographical reference, autobiographical memory (AM) has long been regarded as being episodic in nature. Moreover, autobiographical memory gives researchers the opportunity to study episodic memory using self-relevant material that is more closely related to the current definition of episodic memory (Tulving, 2001, 2002) than that used in most standard tests of episodic memory (Piolino, 2008). The latter rarely make a distinction between the different components (content and context) of episodic memory and do not measure very lengthy retention intervals, autobiographical references or rich phenomenological and idiosyncratic aspects of memory. Interestingly, the assessment of autobiographical memory makes it possible to investigate not only the ability to recall a specific and meaningful personal event, locating it in time and space, but also the ability to travel back into the past and relive specific details of that event which distinguish it from any similar ones. However, as has so often happened in the history of memory conceptions (Baddeley, 2001; Scoville & Milner, 1957), neuropsychological examinations of patients have proved to be an additional source of evidence. Drawing on their pioneering study of the amnesic patient KC, Tulving, Schacter, McLachlan and Moscovitch (Tulving, Schacter, McLachlan, & Moscovitch, 1988; see Rosenbaum et al., 2005, for a review) were among the first to propose a clear distinction between the episodic component of AM (disturbed in KC), containing personal specific events situated in time and space, and a semantic component (preserved in KC), storing general knowledge about one's past, such as the names of acquaintances, personal addresses, generic events and self-concept (Tulving, 1993). This study provided evidence that people can gain mental access to their personal past not only through autonoetic remembering but also through just knowing. Accordingly, semantic memory includes not only general information about the world, but also knowledge about previous personal events and experiences that one can no longer remember. More recently, Conway, Singer, and Tagini (2004) claimed that the retrieval of autobiographical memories depends on a complex, self-driven set of control processes and involves the episodic memory system, which contains event-specific sensory–perceptual–cognitive–affective details, and the long-term semantic self, which contains more abstract autobiographical knowledge (i.e. generic events and conceptual knowledge). Therefore, autobiographical memory is now recognized as being multifaceted, containing a body of general knowledge, as well as unique experiences specific to an individual, which have been accumulated since childhood, and which allow him/her to construct a feeling of identity and continuity (Conway & Pleydell-Pearce, 2000; Piolino, Desgranges, & Eustache, 2000; Wilson & Ross, 2003). When it comes to the relationship between self and memory, Tulving's conception emphasizes the episodic aspects of the self, defending the role of a phenomenological self in the construction and maintenance of subjective continuity in time and personal identity.

The episodic component of AM contains specific personal events, with phenomenological details situated in time and space pertaining to one's self, and presupposes very lengthy retention intervals. Its essence lies in the autonoetic state of consciousness, which enables a personal event to be consciously recollected in its original encoding context and implies mental time travel. Episodic AMs have several core characteristics: they not only concern unique, personal events situated in time and space, but also presuppose phenomenological details (i.e. perceptual, cognitive, affective internal contextual details), self-relevance, the conscious recollection of these events and the rememberer's personal perspective (Brewer, 1996). Visual mental imagery and emotional experience are critical phenomenological characteristics of episodic AM retrieval. Hence, the subjective sense of remembering almost invariably involves some sort of visual (Greenberg & Rubin, 2003) and emotional (Rubin & Berntsen, 2003) re-experiencing of an event. Unlike episodic AM, the semantic component of AM is characterized by a noetic state of consciousness, in which one is capable of retrieving general facts about personal events, but not of reexperiencing specific contexts. Therefore, not all memories that are autobiographical have an autonoetic character mediated by the episodic memory system.

One of the most interesting current debates about episodic memory revolves around whether and how memories change over time. One of the merits of AM studies is that they have painted a much more dynamic picture of memory consolidation, storage and retrieval than strictly "experimental" studies, i.e. those in the Ebbinghaus tradition. There is a strong body of evidence that, rather than being only determined by the length of the retention interval, the distribution of episodic AMs across a long lifespan reflects the survival of vivid memories from late adolescence and early adulthood compared with other remote periods – the so-called reminiscence bump (Rubin, Wetzler, & Nebes, 1986; Rubin & Schulkind, 1997; Rubin, Rahhal, & Poon, 1998) – which represents a potent landmark for the current self (Conway & Pleydell-Pearce, 2000), serving to maintain a sense of identity and continuity in the present. Furthermore, with the passage of time and the repetition of similar events in the phenomenal experience of remembering real-world events, there is a shift away from autonoetic consciousness and towards noetic consciousness, i.e. from episodic to semantic memory (Conway, Gardiner, Perfect, Anderson, & Cohen, 1997; Robinson & Swanson, 1993). This shift is in line with the idea that most features of very long-term memories become semanticized over time (Cermak, 1984), becoming a mixture of semantic knowledge and specific experiences (see also Piolino, Lamidey, Desgranges, & Eustache, 2007; Westmacott & Moscovitch, 2003 for an illustration of this concept in the recollection of names of contemporary celebrities). The nature of AM retrieval and conscious experience depends on the ratio of episodic to semantic elements (see Cabeza & St Jacques, 2007, for a similar view). It has been postulated that the loss of episodic details and the emergence of a conceptual organization cause a "Remember-to-Know" shift over time, as a result of repeated encounters with similar events. It is worth noting that repetition has been shown to influence autobiographical recollection, whether it be "internal" repetition (thinking

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or talking about the same event) or "external" repetition (living through similar events). While external repetition can lead to the decontextualisation or semantization of events, internal repetition can reinforce the persistence of phenomenological details over time (Nadel, Campbell, & Ryan, 2007; Rubin & Kozin, 1984).

The nature of AM across lifetime periods is a critical aspect of the lively argument about the neural substrates of long-term memory consolidation. Despite numerous neuropsychological and functional neuroimaging studies, the neurobiological bases of long-term episodic memory consolidation are still subject to debate (Bright et al., 2006; Mc Gaugh, 2000; Meeter & Murre, 2004). There are two main opposing theories regarding the involvement of the medial temporal lobe (MTL) in long-term memory consolidation. According to the Standard Theory (Bayley, Gold, Hopkins, & Squire, 2005; Squire & Alvarez, 1995), the MTL is involved in the storage and retrieval of declarative memory (either semantic or episodic) for a limited period of a few years. Direct connections have been established between this model and the theory of episodic memory semanticization (see above, e.g. Eustache et al., 2004). The main arguments of the Standard Theory are based on evidence from neuropsychological studies showing diverse profiles of retrograde amnesia depending on the locus of the lesion. In amnesic syndromes where the lesions are concentrated in the MTL or connected regions, the pattern of retrograde amnesia is consistent with the Standard Theory and obeys Ribot's Law (Ribot, 1881), with old memories being better preserved than recent ones. The alternative Multiple Trace Theory considers that while the standard view is valid for semantic information and semanticized memories over time, it is not for lifelong episodic memories (Moscovitch et al., 2005; Nadel & Moscovitch, 1997; Nadel, Campbell, et al., 2007). Rather, the MTL continues to perform its task of recollecting the myriad attributes (time, place, emotional content and perceptual features) of episodic memories no matter how old they are.

Thus, given the multifaceted nature of AM, it is vital to have stringent methods of investigation, especially in order to assess the existence of episodic AM across different time periods, checking not only the ability to represent a specific event and locate it in time and space, but also the ability to recollect specific features of that event via autonoetic consciousness (Moscovitch et al., 2005). In order to investigate the complexity of episodic AM over the course of time and to test the two conflicting models of long-term memory consolidation with respect to the MTL's role in episodic memory retrieval, we carried out a series of cognitive, neuropsychological and neuroimaging studies, using a new tool that has been specially designed to measure the multifaceted episodic features of autobiographical memories and the sense of recollection.

2. A new episodic autobiographical memory assessment based on a subjective sense of recollection: the TEMPau task

Since Crovitz and Schiffmann's ground-breaking study (1974), the introduction of more fine-grained conceptions of AM has considerably improved the way we measure the various contents of AM. However, far too few of the AM assessment tasks currently used in neuropsychology apply a definition of episodic AM based on recollective experience, in accordance with Tulving's current theories. Aside from techniques based on the Galton–Crovitz cue-word paradigm, standardised semi-structured interviews have been developed to examine AMs from different lifetime periods (e.g. Borrini, Dall'Ora, Della Sala, Marinelli, & Spinnler, 1989; Ivaniou, Cooper, Shanks, & Venneri, 2006; Kopelman, Wilson, & Baddeley, 1989). The scoring for autobiographical incidents revolves around the specificity of the event recalled in time and place, and the richness of the description. This kind of scoring adheres to the definition of episodic memory based on its "what," "where" and "when" contents, but ignores the notion of mentally travelling back in time to relive elements of the original experience. Thus, other decisive factors are generally needed to capture the "true" episodic attributes of AM. Some researchers have attempted to unravel the subcomponents of AM, as defined by Tulving, according to the number of contextual details. They claim that in addition to the specificity of the recollection, it is the number of contextual details that makes AM "truly episodic in the sense that one can literally re-experience it" (Moscovitch, Yaschyshyn, Ziegler, & Nadel, 1999; p. 338). In the same vein, Levine, Svoboda, Hay, Winocur, and Moscovitch (2002) proposed investigating recollections from five different lifetime periods, separating the episodic from the non-episodic details (repeated or factual details, metacognitive statements, etc.) by means of a scoring procedure adapted from the Memory Characteristics Questionnaire created by Johnson, Foley, Suengas, & Raye (1988), which lists the qualitative characteristics (e.g. perceptual, spatiotemporal, and emotional) of details about personal events. Particular attention is given to *internal* episodic details that are regarded as reflecting autonoetic experience of the original event. Interestingly, this procedure allows the fine-grained consideration of both episodic and semantic features, even when specific autobiographical events are being recalled. However, it does not rely on the specific mode of subjective experience accompanying the retrieval of memory in the form of a first-person approach (Gardiner, 2001). This other way of distinguishing episodic re-experiencing from semantic familiarity has received relatively little attention in the AM literature, despite the fact that Tulving's conception of episodic memory is inextricably bound up with the subjective phenomenological recollective experience.

It was to remedy this that we designed an original test, known as the TEMPau task (*Test Episodique de Mémoire du Passé autobiographique*, Piolino et al., 2000; for more details, Piolino, Desgranges, Belliard, et al., 2003; Piolino et al., 2006), specifically to assess episodic AM, taking into account not only the specificity of the personal events that are recalled (uniqueness, spatiotemporal location, details), but also the subjective experience of remembering the encoding context. Episodic AM relies not only on the ability to recall a specific event and locate it in time and space, but also on the ability to recollect specific details which distinguish that event from similar ones. As it is possible to rebuild a specific event from one's personal semantic AM without actually reliving sensory–perceptual episodic details, it is vital to gauge the specificity of details from the encoding context through the sense of re-experiencing. The encoding context encompasses time and space (i.e. the specificity of event), sensory–perceptual–affective–cognitive details (i.e. the specificity of details), the subjective experience (i.e. autonoetic consciousness) and the visual experience (i.e. self-perspective) (see Table 1).

Based on existing semi-structured questionnaires (Borrini et al., 1989; Kopelman et al., 1989; Piolino, Desgranges, Benali, & Eustache, 2002), the TEMPau's originality lies in the way it addresses the issue of the state of consciousness and the self-perspective accompanying memory retrieval across the entire lifespan, by incorporating two kinds of subjective measures of episodic re-experiencing (see Fig. 1). Participants are first given precise instructions to recall personal events from five different time periods which occurred only once, at a particular place and date, and lasted several minutes or hours but never more than a day. The subjective reports of memories are then assessed using the Remember/Know procedure (Gardiner, 1988; Tulving, 1985), which makes it possible to differentiate between episodic and semantic memory retrieval, i.e. autonoetic consciousness from noetic consciousness. An alternative response ("Guess") is added in order to ensure that the Know responses do not contain any degree of uncertainty, compared with the Remember responses (Gardiner, Ramponi, & Richardson-Klavehn, 1998). This Remember/Know/Guess procedure, originally used in the context of laboratory learning material

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Table 1
Operational criteria for assessment of episodic autobiographical memory.

Experimenter assessment of content	Specificity of event	Uniqueness Short duration (less than 24 h) Spatial situation Temporal situation
	Specificity of details	Factual* Spatiotemporal** Phenomenological***
Self-assessment of retrieval mode	Point of view (Field/Observer)	Field
	State of consciousness (Remember/Know)	Autonoetic
	Quality of memories	Vividness and number of visual mental images Intensity and emotional valence Frequency of rehearsal

Specific details that only belong to one particular event.
* What, who, causes, circumstances.
** Situation and sequence.
*** Perception, thinking, emotion.

such as wordlists, can be usefully applied to AM retrieval in conditions which tap more complex self-relevant information and the long retention intervals inherent to real life. However, even today, the Remember/Know procedure is seldom used to assess the state of consciousness accompanying remote memories (e.g. Rybash & Monaghan, 1999). Given that one feature of episodic memory is the pulling together into a single episode of what, where, and when something happened, the TEMPau test is designed to probe the different aspects of recollective experience, in particular the factual, spatial and temporal features of memories. Thereafter, a procedure is used to check whether the R responses are infused with the idiosyncratic perspectives, emotions and thoughts of the person doing the remembering. This procedure has previously been carried out in laboratory studies in order to confirm that participants are obeying instructions when they give R responses (see Gardiner, 2001). Besides autonoetic consciousness, the assessment of the rememberer's self-perspective during autobiographical recollection can be based on the viewpoint associated with the

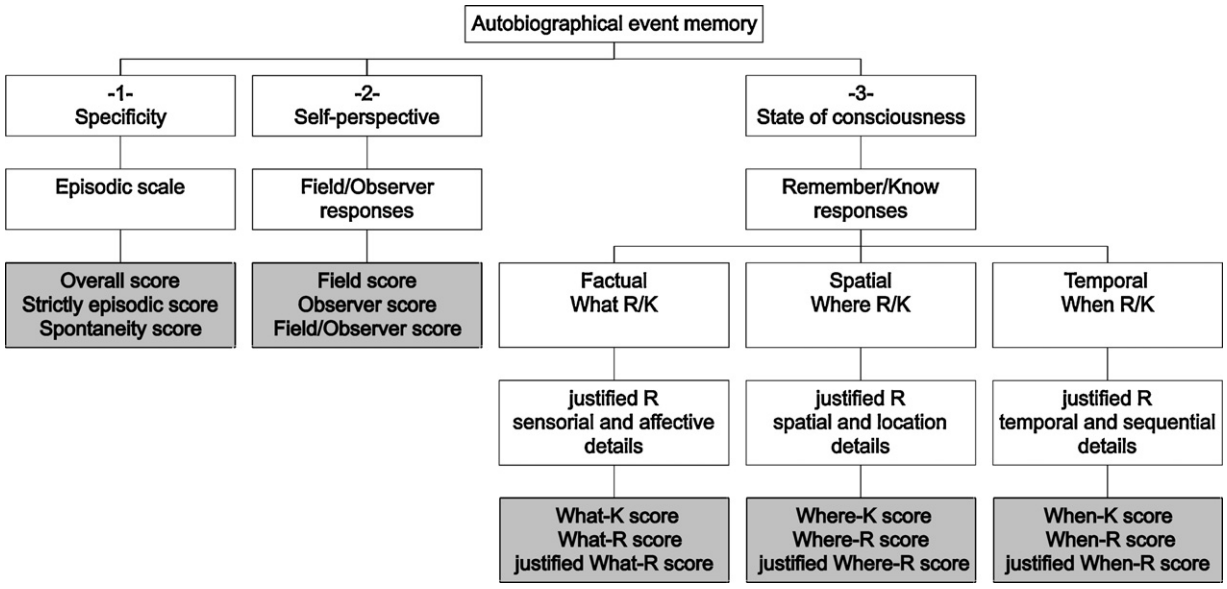

Fig. 1. General organization of the TEMPau task (from Piolino et al., 2006). Description of the Test Episodique de Mémoire du Passé autobiographique (TEMPau) and recorded scores. *Method*: The participants are asked to recall four specific autobiographical memories (or eight for the most recent time period) which have some relevance to their personal lives, from five periods covering their entire lifespan (i.e. 0–17 years old (or childhood and adolescence), 18–30 years old (or young adulthood), more than 30 years old except for the last 5 years (or older adulthood), the last 5 years except for the last 12 months (or relatively recent), the last 12 months (or very recent)). After recall, spontaneous or otherwise, the participants are prompted up to three times to give more details if necessary and/or to be more specific if they have recalled a generic event. After the recall of each event, whatever its level of specificity, the participants are required to report their self-perspective and state of consciousness during retrieval, before the next cue is given (see Field/Observer and Remember/Know). In a field perspective, the participants keep the same viewpoint that they had in the original event, whereas in an observer perspective, the participants see themselves in the event from the viewpoint of an external observer. During the state of consciousness task, separate responses have to be given for the factual (what), spatial (where) and temporal (when) contents of memories. First, they select an Remember response if they can remember the specific episode with its encoding context—in which case, they may virtually relive the previous event (e.g. details such as thoughts, feelings or images related to the recalled event), a Know response if they just know this episode took place but cannot recall any specific event and cannot virtually relive any sensory or affective details pertaining to the recalled event, or a Guess response if they just guess that they probably experienced this episode but neither remember nor know it. Thereafter, a procedure is used to check each Remember response in terms of details (justified Remember). *Scoring*: Each event is scored on a 5-point episodic scale which takes into account the specificity of the content (i.e. single or repeated event), the spatiotemporal situation, and more especially the presence of internal details (i.e. perceptions, thoughts, feelings). Two main total scores are recorded per lifetime period examined: (a) an overall score called the AM score, which includes all the memories (both specific and generic) and corresponds to the classic episodic memory score used in the Autobiographical Memory Interview (Kopelman et al., 1989) and (b) an episodic score, called the EM score which only includes specific and detailed memories scoring 4. A spontaneity score is recorded on a 5-point scale that conversely takes into account the number of cues and/or prompts the participant needed in order to recall a specific event instead of a generic one. The Field/Observer and Remember/Know paradigms and the justified Remember procedure make it possible to record several further scores per period, i.e. the percentage of each type of response.

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mental representations, known as the Field/Observer perspective paradigm (Nigro & Neisser, 1983; Robinson & Swanson, 1993). In total, episodic AM can be characterized as enabling someone to "travel back in time" relive specific events and view these events as they would originally have been seen through his or her own eyes (see also Crawley & French, 2005).

According to Tulving's ideas, justified Remember scores can be regarded as coming closest to the notion of episodic re-experiencing via autonoetic consciousness. Details in this case are deemed to be episodic because they have been re-experienced. The TEMPau task therefore proposes a stringent approach to testing episodic AM retrieval across lifetime periods, based mainly on autonoetic consciousness and self-in-time. The idea here is to consider *how* participants recall matters just as much as *what* they recall (see also Brewer, 1996; Conway & Pleydell-Pearce, 2000; Wilson & Ross, 2003).

3. New insights from the TEMPau task

3.1. Effects of age and time interval on episodic autobiographical memory

Studies of AM across the lifespan have to deal with other factors that are intrinsically related to very long-term intervals, such as the effects of age at encoding and age at retrieval, which can blur the analyses of the effect of time interval *per se*. These factors can be explored using assessment methods that make it possible to evaluate the semantic and episodic components of autobiographical memory in subjects of different ages, by defining time intervals so that retrieval can be studied with a fixed time interval whatever the subject's age. Hence, if the boundaries of each time period under consideration are defined according to the subject's age, it then becomes possible to differentiate between the effects of age, retention interval and age at encoding. Accordingly, like Levine et al. (2002), Piolino et al. (2002) used a semi-structured questionnaire (the precursor of the TEMPau task) to check that episodic recall (i.e. specific and detailed memories) does indeed deteriorate with age and retention interval, whereas semantic recall (i.e. general personal knowledge, such as the names of acquaintances, addresses, jobs, etc.) is characterized by relative invariance. As far as episodic memories are concerned, Piolino et al. (2002) observed (1) the classic temporal distribution of memories (Rubin et al., 1986; Rubin & Schulkind, 1997) characterized by a retention function covering a period of a few years and a clear recency effect, together with (2) the existence of a significant reminiscence bump in subjects of at least 50 years of age and (3) a period of childhood amnesia. In this study, the average encoding ages for the reminiscence bump and childhood amnesia corresponded to 23 and 4 years respectively. The deleterious effects of age concerned the retention function and the reminiscence bump, but not the period of infantile amnesia. Further findings have been obtained more recently using the TEMPau task. First, we demonstrated age effects across all five lifetime periods on the specificity of event recall and spontaneity of retrieval, as well as on the phenomenal experience of remembering—i.e. self-perspective and the state of consciousness (Piolino et al., 2006). While the field perspective and sense of remembering declined with age and remoteness, the sense of just knowing and the observer perspective increased with age and remoteness. These effects concerned the factual, spatial and temporal attributes of memories. These findings therefore suggest that the ability to consciously recollect many specific events and relive the context in which they occurred deteriorates with aging, in line with the findings of classic laboratory tests (e.g., Clarys, Isingrini, & Gana, 2002; Perfect & Dasgupta, 1997; Parkin & Walter, 1992). In older adults, the temporal distribution of Field and Remember responses (justified or otherwise) provided for the temporal content of AM was characterized by a recency effect and by an increase in these responses for distant memories from the 18–30 years old period (i.e. the reminiscence bump). Overall, the main findings highlighted the fact that aging and remoteness not only affect the specificity of details, but also autonoetic consciousness and the self-perspective. The evidence of contrasting temporal profiles for the Field/Observer responses, mirroring the result for the Remember/Know responses, supports the view that there is a shift in the phenomenal experience of remembering real-world events with the passage of time that causes a "Remember-to-Know" and "Field-to-Observer" shift over time (Cermak, 1984; Conway et al., 1997; Linton, 1986). The greatest "Remember-to-Know" shift concerns the temporal attributes of AMs. However, although episodic AMs decrease with age and remoteness, some of them resist because there are self-relevant (e.g. self-defining memories, Conway et al., 2004) and therefore continue to retain the same main features as before, regardless of the person's age (i.e., mental reliving of affective and perceptual details, accessibility, and self-perspectives). Interestingly, we found that age had a gradual effect on the ability to justify Remember responses by recalling specific details, whatever the period and irrespective of the content, although this ability was better preserved for remote time periods than for more recent ones. Therefore, subjective episodic re-experiencing in the form of travelling back in time to relive personal events is more objectively preserved in the most distant past than in the recent past, which may explain why elderly subjects often think their remote memories are better preserved than more recent ones.

Continuing on the theme of the superimposition of subjects' age and the age of their memories, the effect of age at encoding on the recall of the most remote period of life covering the childhood and early adolescence has been further explored using an adaptation of the TEMPau task aimed at school-age children aged from 6 to 13 years (Piolino, Hisland, Matuszewski, Jambaqué, & Eustache, 2007). This study highlighted age-related differences in episodic AM, whereas personal semantic memory (based on general knowledge, such as the names of familiar people or heroes, personal and school addresses, and lessons at school) was characterized by relative developmental invariance. This profile paralleled the developmental dissociation revealed by the Remember/Know paradigm, i.e. autonoetic/noetic consciousness. Increasing age was particularly important in the spontaneity of recall and number of "Remember" responses and their justification in terms of the actual contextual details that were retrieved—factual, spatial and, more especially, temporal details. These findings support the view that mental time travel through subjective time, which allows one to re-experience the past through self-awareness, is one of the last features of autobiographical memory to become fully operational. This is in keeping with Tulving's theory (1985, 2001, 2002) that episodic memory develops later in ontogeny than semantic memory. This assumption has been considered in light of the theory of infantile amnesia originally defined by Freud (1905). According to this, adults are unable to subjectively re-experience the circumstances of early personal events encoded before the age of 5, not because of a problem of retrieval, but because of the absence of truly episodic memory before that age (Wheeler et al., 1997; see also Nelson & Fivush, 2004).

Research carried out more recently in our laboratory has highlighted the role of executive functions in the generative retrieval mechanisms involved in the emergence or impairment of episodic AM retrieval in children or older adults (Piolino, Desgranges, & Eustache, 2008). Moreover, different factors other than age and remoteness, such as emotion and images of the self, are important to study as they are indeed also crucial to AM retrieval in healthy subjects (Libby & Eibach, 2002; Talarico, Labar, & Rubin, 2004) as in patients (see Conway et al., 2004; Guillery et al., 2000; Noël et al., 2008; Williams et al., 2007). For example, while we con-

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firmed in patients with depression a diminution in episodic AMs (i.e. specificity of details, autonoetic consciousness and field self-perspective) compared to healthy controls, all the more concerning positive events (Lemogne et al., 2006), we observed in healthy young adults a relationship between a diminution in episodic AMs (i.e. specificity of details, autonoetic consciousness and field self-perspective), and the cognitive avoidance of intrusive emotional recollections (Lemogne et al., 2009).

3.2. Neural substrates of the re-experiencing of episodic autobiographical memory over time in normal subjects

We have discovered that some relevant episodic AM persist regardless of the time periods being considered, even in older adults. We investigated the neural substrates of these episodic AMs by adopting two complementary approaches, namely activation studies in normal adults and correlational studies between the TEMPau task and resting-state neuroimaging measures.

Yet a great many functional neuroimaging studies have explored the activation triggered by AM tasks in healthy subjects (for reviews, see Cabeza & St Jacques, 2007; Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002; Maguire, 2001; Svoboda, McKinnon, & Levine, 2006). They have found evidence of a large network encompassing the prefrontal, medial and lateral temporal cortices, as well as posterior regions, but yielded controversial results concerning the relationship between the MTL structures and the length of the retention interval. Some studies (e.g. Maguire & Frith, 2003a; Niki & Luo, 2002; Piefke, Weiss, Zilles, Markowitsch, & Fink, 2003) have reported differing degrees of engagement of the hippocampal region in recent and remote AM retrieval, seemingly arguing in favour of the standard model of memory consolidation. Others have provided evidence that semantic memory retrieval involves the MTL regardless of remoteness, which is problematic for the two conflicting theories (Bernard et al., 2004). Most of the other studies failed to find any differential involvement of the MTL as a function of time interval (for reviews, see Cabeza & St Jacques, 2007; Svoboda et al., 2006), thereby contradicting Standard Theory predictions and supporting Multiple Trace Theory ones instead. In some of these studies, methodological confounds may have biased certain results. For instance, in most cases, a questionnaire was administered a few weeks or days prior to the scanning session in order to obtain material for constructing the cues used during scanning to reactivate old memory traces. Only a few studies tried to prevent subjects from reencoding their memories via the hippocampus (e.g. Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004; Okuda et al., 2003).

In our set of studies, we designed specific protocols based on the TEMPau paradigm in order to capture the neural correlates of episodic AM recollection fulfilling five main principles: (1) avoiding the reencoding of memories prior to the scan; (2) promoting the retrieval mode of episodic AM through re-experiencing; (3) probing different lifetime periods; (4) taking into account the dynamics of AM retrieval; and (5) controlling for the episodic nature of memories that are retrieved and the qualities of recollection.

In an initial Positron Emission Tomography (PET) activation study of young adults (Piolino et al., 2004), we examined the mental retrieval of recent (last 12 months) and remote (5–10 years ago) episodic AMs from sentence cues (e.g. a party with your friends within the last year or a special party with your friends that took place when you were between 17 and 20 years of age) controlling for memory access time. The sentence cues were selected from a previous experimental study of AM in healthy subjects on the basis of their likelihood of producing specific detailed AMs in young subjects with the same ease of access regardless of time interval. Prior to scans, the subjects were trained to mentally relive episodic AMs (different from the scanning) with as many episodic details as they could, such as time, location, perceptions and feelings, when they

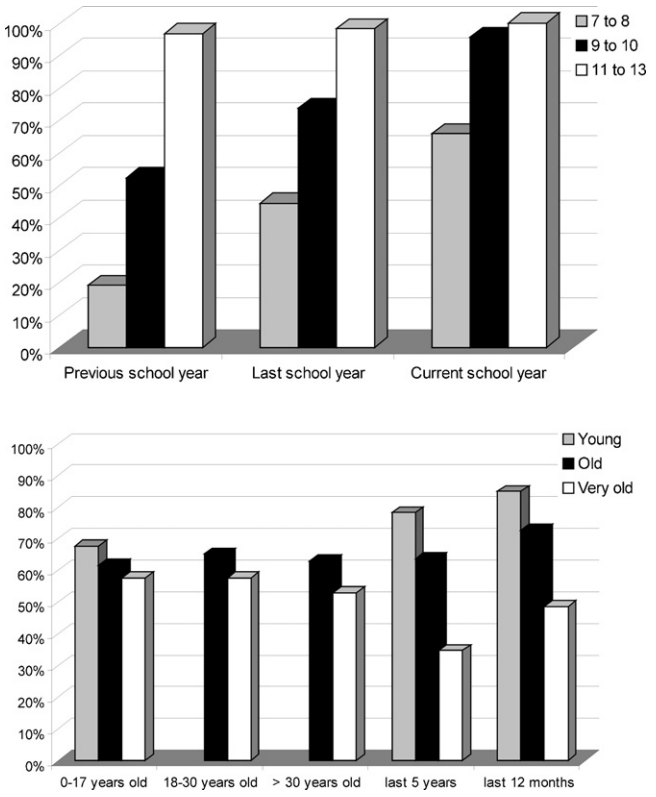

Fig. 2. The percentage of justified Remember responses (mean %) as a function of age group in school-age children (top) and adults (bottom) for each lifetime period (adapted from Piolino et al., 2006; Piolino, Hisland, Matuszewski, et al., 2007).

listened to the sentence cues. After the scans, they were asked to retrieve these evocations again, but this time out loud. The nature of the AMs they retrieved was assessed according to objective measures performed by the experimenters (i.e. specificity and details), as well as to more subjective measures performed by the subjects themselves, regarding the retrieval strategy they had used (verbal or visual), frequency of rehearsal (from none to very frequent), state of consciousness (Knowing or Remembering), vividness of mental visual imagery (from vague to very clear), self-perspective (Field or Observer) and emotion (from none to very intense at encoding or retrieval). The main finding was that the retrieval of both recent and remote episodic AMs was characterized by specificity, autonoetic consciousness, visual imagery and emotion, and principally activated a widespread left-sided network (i.e. left prefrontal, temporal and parietal, anterior cingulate cortex, left fusiform gyrus, left subcortical areas), plus the bilateral posterior cingulate cortex and cerebellum and the bilateral hippocampus. Interestingly, the findings pointed to greater hippocampal activity for remote memories than for recent ones and a predominantly right-sided hippocampal involvement, whatever the remoteness of the autobiographical memories. (Fig. 2).

The second study was designed to explore memories from across the lifespan of older healthy subjects aged approximately 70 years (Viard et al., 2007) and therefore to conduct brain measures of AM recollection for very long retention intervals, lasting decades. The five main principles were the same as before, but we adopted another method of selecting sentence cues and used functional Magnetic Resonance Imaging (fMRI) instead of PET. This time, we asked husbands to describe specific relevant events from their wives' lives, covering the same five time periods as those in the TEMPau task. We were thus able to identify the brain structures involved in the recollection of episodic AMs across the whole lifespan from personally relevant cues, selected by question-

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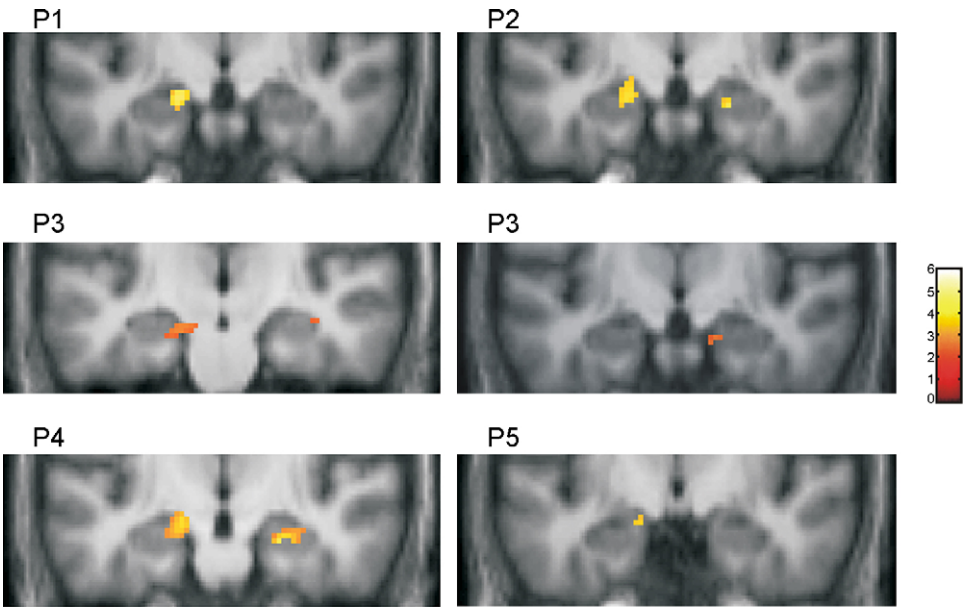

Fig. 3. Images showing results of the small volume correction analysis centred on the hippocampus. Coronal planes indicate left hippocampal activation for P1 (0–17 years old) and P5 (last 12 months) and bilateral hippocampal activation for P2 (18–30 years old), P3 (more than 30 years old), and P4 (last 5 years). Colour scale: voxel *Z*-score values (from Viard et al., 2007).

ing a family member. The findings showed that the recollection of episodic AMs from the five time periods triggered activation within a circumscribed network, including the left hippocampus and superior frontal gyrus, as well as the bilateral precuneus and posterior cingulate gyrus. In addition, the period of the reminiscence bump showed specific activation in the left lateral temporal lobe. Behavioural results indicated that, regardless of the age of the memories, recollection was characterized by specificity (i.e. spatiotemporal uniqueness and details), as well as by an autonoetic state of consciousness and mental visual imagery, attesting to their episodic nature. However, remote memories from young and older adulthood periods (18–30 years old and more than 30), as well as from the last 5 years, were rated more strongly in terms of phenomenological characteristics (emotional intensity, image quality or autonoetic consciousness) than those from both the most remote and most recent periods. These three time periods also triggered the activation of the right hippocampus (Fig. 3). Regardless of the time periods, both anterior and posterior parts of the hippocampus were activated (see Lepage, Habib, & Tulving, 1998; for a discussion on the functional distinction between the anterior and posterior hippocampus in terms of encoding and retrieval processes). New analyses of connectivity between the hippocampus and neocortex have highlighted significant correlations between the activation of the MTL and the activation of the neocortical regions for both recent and remote periods, albeit to a lesser extent for the most recent period (Viard et al., submitted). Interestingly, the latter pattern of results highlighted a bilateral network concerned with episodic AM retrieval. More specially, from the distant past, bilateral hippocampal activation was predicted by other MTL structures (parahippocampal gyrus and amygdala) and by the neocortical regions (lateral temporal cortex and temporal pole).

As a follow-up to our PET activation study, we used another powerful approach—the cognitive–metabolic correlative technique—which requires both cognitive tests and resting-state PET scans to be conducted within a short time interval (a few days at most), and correlations to be performed between these two sets of data across a group of subjects. PET makes it possible to study physiological parameters such as blood flow or metabolism, which are closely related to synaptic activity. It is a well-validated method for mapping the functional neuroanatomy of a given behaviour in neurodegenerative diseases (Desgranges et al., 1998; Desgranges et al., 2002; Eustache, Desgranges, Giffard, de la Sayette, & Baron, 2001; Rauchs et al., 2007; Teipel et al., 2006; see Salmon, Lekeu, Bastin, Garraux, & Collette, 2008, for review). It is particularly useful for establishing cognitive and neurobiological models of human memory, because it allows the mapping of cerebral networks subserving a particular task and can be used to identify regions whose involvement is crucial to the task (see Tulving, Habib, Nyberg, Lepage, & McIntosh, 1999; for a discussion of the concepts of "how sites" and "what sites"). More relevant to the present discussion, the correlative method offers an alternative approach which overcomes some of the methodological limitations to AM neuroimaging studies (e.g. no direct control over the nature of episodic AM activated inside the scanner, the intrinsic difficulty of disentangling reencoding processes from retrieval ones and recall of abstract semantic knowledge from that of specific information) enabling the use of sophisticated cognitive assessments where the nature of memories can be strictly controlled.

The adoption of a cognitive–metabolic approach in order to reveal the neural substrates of AM in healthy subjects was justified by the variability of both cognitive AM performances (Levine et al., 2002; Piolino et al., 2002; Piolino et al., 2006) and brain functions (Coles et al., 2006). This approach is particularly suitable for healthy middle-aged and elderly subjects, who present greater intersubject variability than young subjects (Piefke & Fink, 2005).

The aim of our neuroimaging study of healthy subjects was to pinpoint the brain structures whose synaptic function subserves the recollection of lifetime episodic AM, establishing correlations between resting regional Cerebral Blood Flow (rCBF) measured with PET and AM indexes regarding rich episodicity (i.e. the recollection of specific events with episodic details corresponding to justified Remember responses) and spontaneity (i.e. the retrieval of memories without retrieval support) obtained separately using the TEMPau task (Piolino et al., 2008). The results of 12 healthy middle-aged subjects showed that the majority of memories involved a field perspective, gave rise to a sense of remembering which was justified in terms of specificity and details, and were relatively spontaneously retrieved, regardless of their remoteness. Based on *a priori* hypotheses regarding the involvement of the frontotemporal neocortical structures and hippocampal region in AM retrieval (see

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Cabeza & St Jacques, 2007; Conway et al., 2002), we first extracted the mean rCBF for each anatomical volume of interest selected from a bilateral set of regions of interest covering the left and right frontal and temporal lobes. Our paradigm gave us the opportunity to single out two distinct aspects of AM retrieval, by recording the generative processes (i.e. spontaneity index) and the recollection based on autonoetic consciousness with reliving of episodic details (i.e. episodicity index). The main results indicated that the rCBF values for the right hippocampus predicted the episodicity index (unlike the index of semantization, based on Know memories) regardless of the content (but spatial > factual > temporal details) and age of the memories, while that of the left medial orbital frontal gyrus predicted the index of spontaneity, again for every lifetime period. Second, a voxel-based analysis of the whole brain using an exploratory approach confirmed these striking relationships between episodic AM and rCBF in the medial temporal regions, including the hippocampus, and between the spontaneity of access to specific memories and rCBF in the frontal regions (see Fig. 4A1 and A2). Other correlations for the episodicity index concerned a network which bilaterally encompassed the hippocampus, parahippocampus, precuneus, lingual gyri and thalamus, regardless of the period, with additional involvement of temporal and prefrontal neocortical regions for some of these periods. Concerning the spontaneity index, the main correlations concerned the prefrontal cortex bilaterally, more specifically the orbitomedial surface (ventromedial part of Brodmann Area 10; medial parts of BA 11 and 47). Further SPM results (Fig. 5) showed that the field perspective was mainly correlated with the right MTL (hippocampus and parahippocampus) and lingual gyrus and left temporal pole, while observer memories were mainly correlated with the left dorsolateral and superior frontal gyri and bilateral posterior areas (cuneus and occipital lobe).

Overall, these findings for healthy subjects emphasize the notion that the hippocampus and neocortical regions are permanently involved in episodic AM retrieval, regardless of remoteness. Right-sided or bilateral involvement of the hippocampus characterizes rich episodic AM recollection (see Section 4).

3.3. *Neural substrates of the re-experiencing of episodic autobiographical memory over time in brain-damaged patients*

Some memory diseases have a massive impact on AM, especially its episodic subcomponent (for reviews, see Conway & Fthenaki, 2000; Kopelman, 2000; Kopelman & Kapur, 2001). Studies of lesions in non-demented patients have emphasized the role of frontotem-

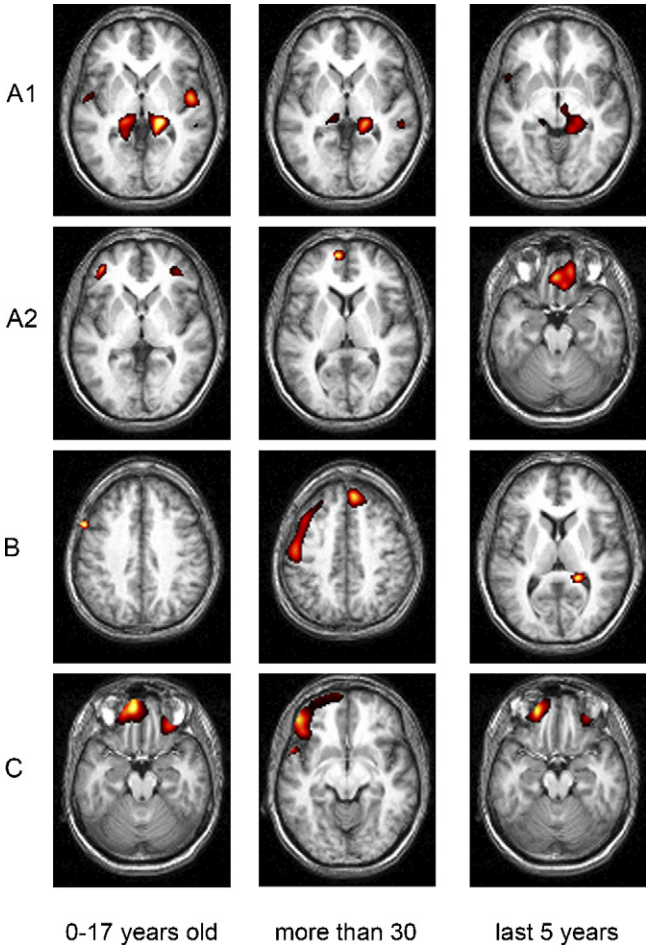

Fig. 4. SPM T-maps of significant correlations between TEMPau scores and resting brain measures (PET) for three lifetime periods. (adapted from Eustache et al., 2004 (B); Piolino, Chételat, Matuszewski, et al., 2007 (C); Piolino, Desgranges, Hubert, et al., 2008 (A1 and A2))—(A1 and A2). Results in normal middle-aged subjects for the correlation between cerebral blood flow (CBF) and the episodicity (based on autonoetic consciousness) and spontaneity indices ($p < .005$ uncorrected, cluster size $k > 100$)—(A1 and A2). Results in early to moderate Alzheimer's disease (AD) for correlation between FDG uptake and the AM index ($p < .01$ uncorrected, cluster size $k > 80$)—(B). Results in frontotemporal dementia (FTD) for correlation between FDG uptake and the AM index ($p < .005$ uncorrected, cluster size $k > 100$)-(C).

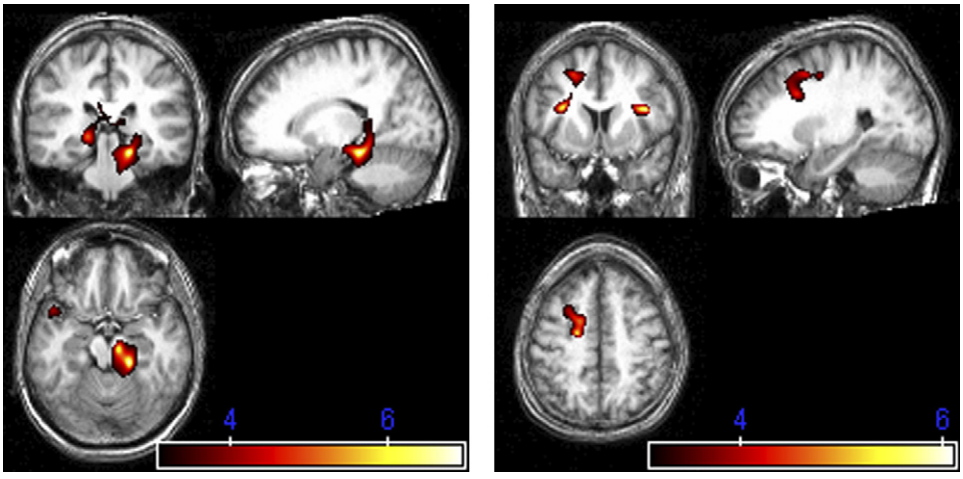

Fig. 5. SPM T-maps of significant correlations between self-perspective in the TEMPau task and resting brain CBF measures (PET): field (in the left) and observer (in the right) viewpoints in healthy elderly subjects ($p < .005$ uncorrected, cluster size $k > 100$).

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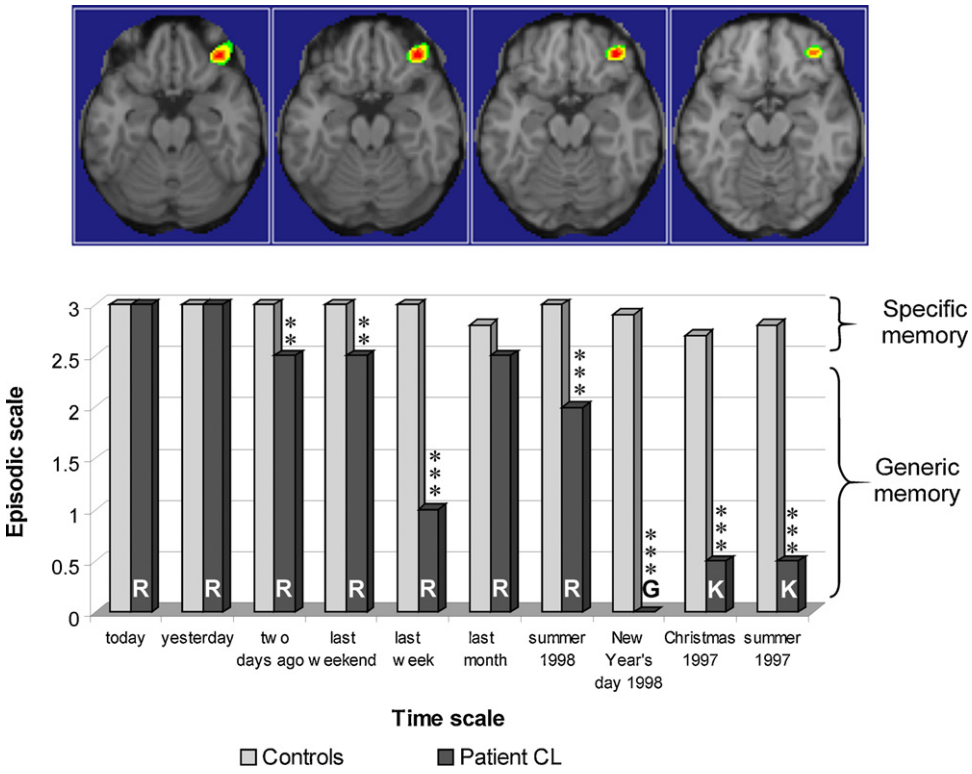

Fig. 6. SPM T-maps showing the significant hypometabolism found in Patient CL compared to normal controls (PET-FDG, $p < 0.001$ uncorrected) projected in transverse position and TEMPau CL's performances (adapted from Piolino et al., 2005). *Caption*: Detailed scoring for each of the post-onset memories (no pre-onset memories) recalled by CL in the TEMPau task (from the last12-month-period, and Christmas and summer 1997 from the last 5-year-period) using a fine-grained 6 half-point episodic scale, shown alongside controls' results (mean rating scores), from the shortest interval (today) to the most distant interval tested, and CL's subjective Remember, Know or Guess responses accompanying each of his recollections. Data shown are the mean rating scores for controls from each question tested on the patient. CL's raw scores are shown with statistical significance according to *Z*-scores (pathological score: $^{**}p < 0.01$; $^{***}p < 0.001$).

poral areas in AM disruption, especially the right side (for reviews, see Markowitsch, 1995; Kopelman, 2000). For example, Patient ML (Levine et al., 1998) suffered from organic focal retrograde amnesia after a head injury resulting in right-sided frontal damage (BA 47) that involved the uncinate fasciculus and may have disconnected the frontal and temporal structures. Using the TEMPau task, the right prefrontal cortex was also found to be involved in a case study of disproportionate retrograde amnesia (Piolino et al., 2005). Patient CL manifested a sudden and persistent total loss of personal identity in the context of clinically documented good everyday memory and normal neuroanatomical data (CT scan, MRI). When compared with an age-matched control group, the hypometabolism was found to be entirely restricted to the right orbitofrontal cortex (BA 11/47, Fig. 6). CL's state of mind was "a blank" whenever he tried to think about his past. Even his post-onset episodic AMs were fragile: he retained a subjective sense of remembering for the last few days and weeks, but was unable to recollect more distant personal events through mental time travel, even those that were particularly self-relevant (e.g. his "first" Christmas).

The mechanisms by which episodic AM retrieval is disrupted and their connection with the frontotemporal structures have also been studied in demented patients with cortical dysfunction. Our neuropsychological data revealed strongly contrasting profiles of autobiographical retrograde amnesia according to the type of dementia (Piolino, Desgranges, et al., 2003), in keeping with other studies (e.g., Ivaniou et al., 2006; Nestor, Graham, Bozeat, Simons, & Hodges, 2002). More specifically, in Alzheimer's disease, which preferentially affects the medial temporal lobe in the early stage of dementia, we observed temporally graded memory deficits obeying Ribot's Law, with remote memories being better preserved than recent ones. Nevertheless, a fine-grained analysis showed that relatively preserved remote memories in Alzheimer's disease were, in fact, semanticized memories, with the result that episodic AM had an entirely flat gradient. In semantic dementia, characterized by mainly external temporal lobe lesions with relative sparing of the medial temporal lobe, our data revealed memory loss with a reverse gradient. However, an assessment based on a sense of recollection (Remember responses) unconstrained by verbal abilities brought to light a relative preservation of episodic AM in early-stage semantic dementia, regardless of the lifetime period (see also Moss et al., 2000; Piolino, Belliard, Desgranges, Perron, & Eustache, 2003; Westmacott et al., 2001 for similar findings). Lastly, in the frontal variant of frontotemporal dementia, results showed memory loss without any clear temporal gradient (see also Matuszewski et al., 2006). Episodic memories in their strictest definition (i.e., unique, detailed, specific in time and space) were impaired, whatever the time interval considered in the three groups, though memory loss was global in Alzheimer's disease and frontotemporal dementia, and temporally graded in semantic dementia, sparing the most recent period. These results demonstrate that autobiographical amnesia varies according to the nature of the memories under consideration and the locus of cerebral dysfunction. We have discussed these profiles of autobiographical amnesia in the light of the two competing models of long-term memory consolidation and recent conceptions of autobiographical recollection (Piolino, Desgranges, et al., 2003). Principally, the existence of a temporal gradient for semanticized AM but total episodic retrograde amnesia (regardless of the period) resulting from MTL damage in early Alzheimer's disease supports the Multiple Trace Theory rather than the Standard Theory.

The main objective in conducting a series of neuroimaging studies in neurodegenerative diseases was to further unravel the neural bases of clear-cut temporal gradients in AM deficits, according to

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the type of dementia. We used the same approach as we had done in the healthy elderly adults, looking for correlations between the resting-state cerebral measure and temporally graded AM scores in order to identify the brain structures whose synaptic dysfunction subserved the impairment. To this end, we studied a group of 17 Alzheimer's disease patients with mild to moderate dementia (Eustache et al., 2004). We administered an abridged version of the TEMPau task, assessing just three broad time periods (childhood and teenage years (0–17 years old), middle age (more than 30 years old) and the previous 5 years), and measured resting cerebral metabolic rate of glucose using PET (resting normalized fluorodeoxyglucose uptake). The findings showed diverse correlation patterns according to the time period being tested: the correlations were restricted to the left middle frontal gyrus for the teenage and childhood period, the bilateral prefrontal cortex (bilateral superior, bilateral middle and right inferior gyri) for the middle-age period, and the right hippocampus and right frontal and temporal gyri for the last 5 years (see Fig. 4B). The data showed that the hippocampus became disengaged from the retrieval of remote AMs, which became semantic instead of episodic. These findings are consistent with both models of memory consolidation, in that the latter share the notion of the temporary role of the hippocampus in semanticized memories. In the same vein, the shift from right to left frontal regions as the time interval increases may reflect the move away from an episodic retrieval mode towards a more semantic one (see Hemispheric Encoding/Retrieval Asymnetry model, Tulving, Kapur, Craik, Moscovitch, & Houle, 1994).

In order to examine the specificity of the neural bases of AM impairments depending on the type of neurodegenerative disease, we applied the same methodology, this time examining 5 lifetime periods, to a group of 20 patients with frontotemporal dementia (Piolino, Chételat, Matuszewski, et al., 2007). Behaviourally, the frontotemporal dementia patients' performances were relatively similar to those of the Alzheimer's disease patients, in that they provided generic memories instead of event-specific sensory–perceptual–affective details, but without the temporal gradient, and displayed deficits in the sense of reliving and self-perspective during retrieval (i.e. providing more Know and Observer responses). This pattern was very similar to that found in a group of patients with traumatic brain injury, who manifested deficits in specificity, autonoetic consciousness and field perspective across all the lifetime periods (Piolino, Desgranges, Manning, et al., 2007). The investigation of the mechanisms responsible for AM deficits in frontotemporal dementia related not only to executive functions, as in our traumatic brain injury group, but also to semantic verbal skills, as in semantic dementia patients (see Matuszewski et al., in press). The cognitive–metabolic correlations in frontotemporal dementia (Fig. 4C) revealed that the AM deficits stemmed mainly from the dysfunction of the left-sided orbitofrontal regions (BA 11) and, to a lesser extent, that of the left-sided dorsolateral (BA 6), frontal and temporal neocortical regions, whatever the time period. Additional analysis showed that deficits in specific memories were correlated with a dysfunction of the left orbitofrontal areas, whereas the impaired production of generic memories was correlated with a dysfunction of the left temporal pole.

We were therefore able to confirm the existence of a specific pattern of correlations in frontotemporal dementia compared with Alzheimer's disease, highlighting the effectiveness of the correlative approach in shedding light on the mechanisms underpinning different profiles of AM deficits. More specifically, the mechanisms of deficits in Alzheimer's disease (characterized by a temporal gradient) were found to involve the hippocampus for recent AMs (i.e. mainly anterograde memories) and the prefrontal cortex for remote ones. By contrast, our findings support the view that AM deficits in frontotemporal dementia (characterized by a flat gradient) mainly stem from orbital prefrontal and lateral temporal dysfunction, regardless of the time period. The pattern of correlations therefore underlines the similarity of the mechanisms behind deficits in anterograde and retrograde memories in frontotemporal dementia, unlike Alzheimer's disease.

Overall, these studies yielded arguments in favour of the role of the MTL, and more specifically the hippocampus, in the retrieval of recent and remote episodic AMs, unlike the retrieval of semantic AM, in keeping with the Multiple Trace Theory. We attempted to find further arguments for Multiple Trace Theory in non-demented patients with focal lesions within the MTL. Neuropsychological investigations designed to examine the extent of retrograde AM deficit in unilateral MTL lesions, be they single-case or group studies, have proved controversial, especially regarding episodic AM. In collaboration with a research group specializing in epileptic patients (Noulhiane, Piolino, Hasboun, Baulac, & Samson, 2007; Noulhiane, Piolino, Hasboun, Baulac, & Samson, 2008), we carried out a study of 22 patients who had undergone a left- ($n = 12$) or right-sided ($n = 10$) MTL resection for the relief of epileptic seizures, using a correlative approach based on the TEMPau and precise MRI volumetric measures of the remaining tissue of the temporal lobe, including different regions of the MTL (i.e. hippocampus, entorhinal, perirhinal and parahippocampal cortices), temporopolar, and the lateral temporal lobe (i.e. superior, middle and inferior temporal gyri). Both patient groups displayed impaired episodic AM retrieval across all time periods, compared with matched control subjects, reflecting particular difficulty in producing specific and detailed memories, associated with poor autonoetic consciousness, as revealed by the small number of justified Remember responses across all periods. This result was in keeping with some other recent studies, which have shown that the famous Patient HM (Steinvorth et al., 2005) who underwent bilateral MTL removal to control intractable epilepsy (Scoville & Milner, 1957), and groups of patients with either right or left MTL damage (Viskontas, McAndrews, & Moscovitch, 2000) were in fact equally deficient in episodic AM across their entire lifespan, without any temporal gradient, whereas personal semantic and generic memories were spared. That said, we noticed that the patients with a right-sided resection had more difficulty in recollecting episodic details from the reminiscence bump period (18–30 years old), whereas the patients with the left-sided resection experienced particular difficulty regarding the most recent period. Analyses of correlations between MRI volume measures of temporal lobe structures and autobiographical memory scores showed that there was no such correlation with the volumes of the lateral temporal lobe structures, but revealed that right MTL structures predicted episodic AM scores regardless of remoteness. Therefore, these findings confirmed the permanent role of MTL in episodic AM retrieval in keeping with the Multiple Trace Theory.

3.4. Deficits in the re-experiencing of episodic autobiographical memory through time travel and the sense of self

As AM provides knowledge of one's experiences across time, enabling the integration of past and present selves, AM deficits predict a weakened sense of self (Bluck, 2003; Conway et al., 2004). However, it can be noted in our AM studies that age-related deficits in AM fail to weaken self-coherence in healthy elderly participants (Duval, Eustache, & Piolino, 2007) as opposed to our patients with psychiatric diseases such as depression (Lemogne et al., 2006) and schizophrenia (Danion et al., 2005), and neurological diseases such as Alzheimer's Disease, or frontal lobe damage who present severe retrograde amnesia with loss of self-identity. One of our studies (Piolino et al., 2006) has provided further evidence that, despite episodic AM deficits in aging, the preservation of (a) personal semantic memory, which is a fundamental component of personal identity (Conway et al., 2004; Tulving, 1993; Wilson & Ross, 2003), (b) the subjective sense of remembering for the remote

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past, and (c) some episodic memories, enables healthy older people to "travel back into their past", thereby ensuring a sense of identity and continuity in time.

We also observed that patients with frontal lobe damage or medial temporal lobe damage had a selective deficit in episodic AM, with relative preservation of semantic AM, and an impoverished ability to consciously recollect their past, even though they knew about their past, giving a clear example of the distinction between autonoetic remembering and noetic knowing. The reverse dissociation has been described in rare cases of patients with early-stage semantic dementia, who lose some personal semantic knowledge but are still able to recollect some episodic details (Piolino, Belliard, et al., 2003). More generally, our patients with episodic AM disruption presented deficits in specificity, autonoetic consciousness and self-perspective, and were hampered in their ability to "travel back in time", relive specific events and view these events as they would originally have been seen through their own eyes. Like Patient KC, they still had a sense of personal identity, in that they could answer the question "Who am I?": they knew their name, those of family, friends and colleagues, some general information such as that given in a curriculum vitae, and also repeated personal events. However, they were frequently unable to recollect the slightest specific personal event, even the most relevant and emotional ones. Depending on the extent of the episodic AM disruption, their personal identity was more or less devoid of "intimacy", which has been regarded as one of the main phenomenological properties of recollection since James (1890). With the progression of dementia and the additional impairment of semantic AM, deficits eventually extended to a loss of conceptual self (see Addis & Tippet, 2004). This observation is significant at two levels: first, it clearly confirms a dissociation in autobiographical memory between episodic and semantic aspects, and secondly, it clearly demonstrates that personal identity does not only involve conceptual self-knowledge (Conway et al., 2004), but also relies on episodic attributes, such as autonoetic consciousness, which allow individuals to remember the past in an experiential way. Indeed, one of the main functions of episodic AM is not only to adapt itself to the present but also to maintain continuity of self in subjective time. It is the phenomenological self that gives us the ability to remember specific instances which illustrate why and how we know who we are.

4. General discussion

We conducted a series of studies of episodic memory based on a special method for assessing episodic AM across lifetime periods which placed the emphasis on the central attribute of episodic memory, namely the autonoetic re-experiencing of past events via subjective mental time travel. With regard to the neural substrates of episodic AM over time, these studies broadly highlighted the cerebral network that was recently identified in the review by Cabeza & St Jacques (2007). More specifically, they clarify the network's role in different aspects of re-experiencing AM through mental time travel and its links with other cognitive functions. We begin by discussing the convergent evidence for the constructive and dynamic nature of episodic AM over time, emphasizing the role of prefrontal and external temporal regions. We then go on to evoke the role of the MTL, and more especially the hippocampus, in episodic AM retrieval, focusing on changes over time and the phenomenological attributes.

4.1. The constructive and dynamic nature of episodic AM across time

Our cognitive findings in children and elderly subjects and our neuropsychological and neuroimaging findings clearly confirm that the episodic and semantic subcomponents of AM can be dissociated, but are also closely linked, at both cognitive and neural levels; they have common and unique processes. This is in line with neuroimaging studies that have emphasized between-systems similarities and within-system differences during episodic memory and semantic memory (Burianova & Grady, 2007; Levine et al., 2004; Nyberg, Forkstam, Petersson, Cabeza, & Ingvar, 2002). More specifically, our developmental outcomes (in children and elderly subjects alike) confirm that episodic memory is a "late-developing, and early-deteriorating past-oriented memory system, more vulnerable than other memory systems to neuronal dysfunction" (Tulving, 2002, p. 5).

Furthermore, the study of the cognitive mechanisms behind episodic AM disruption has provided evidence in support of the multifaceted nature of episodic AM retrieval and construction, which calls on multiple processes: gaining access to sensory–perceptual–cognitive–affective specific details elicits visual imagery and the autonoetic experience of mentally "reliving" a unique past event, and involves executive processes which interact with personal semantic knowledge. Accordingly, the neuropsychological data of patients with frontotemporal dementia or semantic dementia clearly show that AM disruption stems from a deficit in the generative/construction processes that trigger episodic AMs, processes which are closely linked to executive and semantic functions subtended by frontal and anterior temporal regions (Conway & Fthenaki, 2000; Conway et al., 2002).

Otherwise, neuroimaging studies of healthy subjects have revealed that the recollection of episodic AMs associated with a sense of remembering requires retrieval processes that are reliant on the prefrontal cortex and lateral temporal lobe for generative and semantic processes, but also on the medial temporal lobe for recollection (autonoesis, emotion, self-perspective), and parieto-occipital regions such as the cuneus/precuneus for mental visual imagery. The data suggest that episodic AMs are triggered in the prefrontal cortex and generated through information stored in networks located near the posterior brain via the hippocampus, which plays a special role in recollecting and binding all the multifaceted attributes of episodic AM (e.g. images, feelings, see below). This is in keeping with neuropsychological studies that have shown that AM is disrupted by frontal and/or temporal lobe lesions (see Conway & Fthenaki, 2000; Kopelman & Kapur, 2001; Markowitsch, 1995, for reviews), by more posterior lesions (Greenberg & Rubin, 2003) or by their disconnection (Levine et al., 1998; Piolino et al., 2005). At the cognitive level, breakdowns in executive function, but also in episodic and semantic memory, can play a major role in episodic AM disruption, as comprehensively illustrated by the contrasting patterns of autobiographical amnesia in the three neurodegenerative diseases we explored.

We also found that specificity, the subjective sense of remembering and the original field perspective, all of which are deemed to be critical features of episodic memory, are prone to fading and decay over time. However, even if the semantization of episodic memories over time does indeed occur, some lifelong episodic AMs resist this trend. At the neural level, we found that semanticized AMs ceased to depend upon the MTL (i.e. in studies of healthy subjects and Alzheimer's disease patients), while episodic AMs remain under the influence of the MTL and MTL-neocortical links. Of particular interest, we noted the presence of external temporal lobe activation or correlation, clearly demonstrating the increasing role of semantic processes in episodic AM retrieval over time and, more generally, the dynamic relationships between both subcomponents of AM. For example, the 18–30 years old period, which concerns the reminiscence bump, containing vivid and self-relevant phenomenological episodic memories, was characterized by the additional involvement of the right superior temporal pole and superior/middle temporal gyrus. This period includes events encoded during adolescence and young adulthood which are par-

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ticularly well-remembered by subjects over 40 years old and are relatively well-protected from the deleterious effects of time and age (Piolino et al., 2002; Piolino et al., 2006). Hence, this result stresses the role of semantic knowledge in accessing episodic memories from the reminiscence bump which are particularly critical to one's sense of identity (Conway & Pleydell-Pearce, 2000; Fitzgerald, 1996). Leaving aside the reminiscence bump, the temporal pole and lateral temporal regions correlated with MTL regions and episodic re-experiencing during the retrieval of recent and remote periods alike. The role of both external temporal regions in episodic AM is consistent with the fact that lesions to the temporopolar region may cause focal retrograde autobiographical amnesia (Wheeler & McMillan, 2001) as this region is deemed to act as a convergence zone, binding information from the hippocampal structures and posterior association regions (Damasio, 1989; Markowitsch, 1995). Moreover, there is evidence to link the functions of the lateral temporal lobes and temporal pole to personal semantic memory processes (for a review, see Svoboda et al., 2006). Lastly, we were able to demonstrate that the percentage of generic memories provided by frontotemporal dementia patients was correlated with the metabolism of the left temporal pole. Overall, our findings substantiate the notion that executive and both episodic and semantic memory processes are integral parts of episodic AM recollection, because of their special role they play in constructing an AM trace (Conway et al., 2002; Levine et al., 2004; Svoboda et al., 2006).

Therefore, episodic AM studies make it possible to look at episodic memory representations and processes from a much more dynamic perspective than the recall of stimuli presented in the laboratory. Several studies have demonstrated that the conscious recollection of autobiographical events involves common but also unique processes compared with this kind of recall (Nyberg et al., 2002; Burianova and Grady, 2007). Our studies were specifically designed to enlight the evolution and reorganization of personal experiences over the course of time and to unravel the complex mechanisms of episodic AM retrieval pinpointing the role of the frontal and medial temporal structures in these mechanisms.

4.2. The role of left prefrontal regions in episodic AM retrieval

As far as the role of the prefrontal cortex and executive functions in episodic AM retrieval deficits is concerned, our neuropsychological and neuroimaging examinations of frontotemporal dementia and traumatic brain injury patients (as well as normal elderly subjects) provide rigorous convergent evidence, regardless of the lifetime period. This is in line with the literature on autobiographical amnesia in patients with focal lesions to the frontal lobe and the findings of neuroimaging studies of normal subjects, which have shown that the frontal lobe plays a crucial role in episodic memory and autonoetic consciousness (Wheeler & Stuss, 2003; Wheeler et al., 1997). These data are not only consistent with the role of the prefrontal cortex in self-referential processes, but also with its role as a working-with-memory structure that is involved in strategic aspects of retrieval, such as establishing a retrieval mode and goals, initiating and guiding search, and monitoring and verifying the memories that have been retrieved (for reviews, see Cabeza & St Jacques, 2007; Gilboa, 2004).

Our findings confirm the constant left-sided recruitment of the prefrontal cortex in AM retrieval, even concerning its episodic subcomponent, which contrasts with the right-sided involvement in episodic memory highlighted by laboratory paradigms. Gilboa (2004) has demonstrated that the activation of the right prefrontal cortex (BA 9/46/10) is rarely observed in AM studies, as opposed to episodic memory studies based on laboratory paradigms. Laboratory activation studies of healthy subjects have shown that the right prefrontal cortex subtends the retrieval of episodic information (regardless of its verbal or visuospatial nature), whereas the left prefrontal cortex subtends the retrieval of semantic information (see Hemispheric Encoding/Retrieval Asymmetry model, Habib, Nyberg, & Tulving, 2003; Tulving et al., 1994). Several interpretations have been proposed for this preferentially left-sided prefrontal cortex activation observed in AM studies (for a review, see Cabeza & St Jacques, 2007; Gilboa, 2004), but we adhere to the view that it may depend on the nature of generative AM retrieval, which relies on both executive and semantic processes, even when vivid episodic AMs are triggered (Conway et al., 2002). This is well in agreement with the results of Nyberg and his collaborators demonstrating that AM retrieval, semantic memory and working memory overlap in left prefrontal cortex (Nyberg et al., 2003).

Our results stressed the involvement of different parts of the left prefrontal cortex which may reflect the intervention of distinct processes (see Badre & Wagner, 2004; Christoff & Gabrieli, 2000; Petrides, 2000). While our activation studies have mainly established the existence of left dorsolateral prefrontal activation, our correlational studies of healthy subjects and frontotemporal dementia patients have pinpointed the critical role of the left orbitomedial prefrontal cortex (BA 11/47) and, to a lesser extent, that of the left dorsolateral prefrontal cortex (BA 6/45). Our findings regarding the left dorsolateral cortex are consistent with its secondary involvement in AM reconstruction (Svoboda et al., 2006), and suggest that this region is mobilized when high demands are placed on monitoring processes for certain time periods (e.g. the most remote one). As regards the orbitomedial (or ventromedial) prefrontal cortex, this is one of the most ubiquitous activation sites in AM neuroimaging studies. In fact, although both orbital and dorsolateral areas are associated with executive functions (Cabeza & Nyberg, 2000; Collette & Van der Linden, 2002), the role of the left orbitofrontal cortex seems to be more crucial in autobiographical retrieval (Gilboa, 2004; Svoboda et al., 2006). This could be due to its involvement in behavioural regulation, emotion or inhibition processing and, of particular relevance here, in the generative retrieval processes activated in the TEMPau task. Our AM task probably prompts the assessment of internally generated information and a number of self-referential processes (i.e. representation, monitoring, assessment and integration of material of a personally relevant nature, Cabeza & St Jacques, 2007; Northoff & Bermpohl, 2004), and these mainly involve this prefrontal region. Moreover, Brodmann areas 11 and 47 are closely connected to the limbic structures (Wheeler & Stuss, 2003), this connection being crucial to episodic AM retrieval (i.e. access attempts and recollection). Therefore, we suggest that the major involvement of the left orbitomedial prefrontal cortex in the TEMPau task reflects the critical role of self-referential representation in AM strategic retrieval processes.

Nevertheless, supplementary analyses (based on connectivity or correlation methods and on hypometabolism in one case study) performed in both types of neuroimaging studies indicated a more bilateral involvement of the prefrontal cortex in episodic AM retrieval. This right-hemispheric prefrontal cortex involvement fits in better with the functional role of this region observed in the episodic memory retrieval task (Desgranges et al., 1998; Tulving et al., 1994). In particular, the right orbitomedial prefrontal cortex matches one of the three right prefrontal cortical sites shown to be involved not only in the establishment and maintenance of episodic memory in the "retrieval mode" (Lepage, Ghaffar, Nyberg, & Tulving, 2000), but also in the adoption of self-perspective when remembering past episodes (Northoff & Bermpohl, 2004) and in affect-laden autobiographical memory (Markowitsch, Vandekerckhove, Lanfermann, & Russ, 2003). However, an increasing number of activation studies have detected bilateral prefrontal recruitment during episodic AM (Greenberg et al., 2005), possibly due to the use of longer retrieval times (approximately 20 s). Based on electrophysiological findings, Conway et al. (2002) suggested that left prefrontal activation first appears during the retrieval phase and reflects ini-

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tiation processes, whereas right prefrontal activations arise later, along with those of the temporal and posterior regions, when a memory is held in mind, and reflect access to episodic details via autobiographical knowledge (i.e. personal semantics), as well as re-experiencing via autonoetic consciousness.

4.3. The permanent role of the medial temporal lobe in the recollection of episodic autobiographical memories

The close concordance between our neuropsychological and functional neuroimaging (activation or correlations) data has highlighted the involvement of the MTL—and more precisely the hippocampus—in episodic AM across time. Using strict criteria for controlling the episodic features of AM, and avoiding certain methodological biases prevalent in neuroimaging studies, our present results demonstrate that the recollection of episodic memories is dependent upon the hippocampus whatever their age, unlike that of semanticized memories (i.e. memories of generic events or memories associated with Know responses). Importantly, episodic AMs are characterized by spatiotemporal specificity, but also by autonoetic consciousness, visual imagery and emotion, all of which are critical features of episodic memory. We therefore emphasize that hippocampal involvement is not only related to the specificity of memories, but also to the sense of "mental time travel" and phenomenological re-experiencing (Tulving, 2002; Wheeler et al., 1997). Our studies confirm previous findings that have revealed not only a common memory retrieval network supporting all AM types, but also unique regions dedicated to either episodic or semantic AM (Levine et al., 2004; Maguire & Mummery, 1999), supporting a functional neuroanatomical dissociation between episodic and semantic autobiographical memory. The critical role of the hippocampus in autonoetic consciousness may seem surprising, given that autonoetic re-experiencing is regarded as a function that is most likely to be subserved by the frontal lobes. Nonetheless, this involvement is in keeping with several studies suggesting that MTL structures, notably the hippocampus, do indeed play a part in this phenomenon (Moscovitch et al., 2005; Tulving & Markowitsch, 1998).

The involvement of the hippocampus in episodic AM retrieval whatever the lifetime period argues against the Standard Theory of consolidation and instead supports the Multiple Trace Theory, which states that the MTL is involved in the mechanism that reactivates all the neocortical regions where the multifaceted components of episodic memories are represented, regardless of the passage of time (see Section 1). Further strong arguments are additionally provided, as we underline the permanent nature of the connectivity between the MTL and neocortex (more specifically the temporal region) in healthy subjects, both for remote and recent episodic AMs, as predicted by the Multiple Trace Theory (Moscovitch et al., 2005; Nadel, Winocur, Ryan, & Moscovitch, 2007; Nadel, Campbell, et al., 2007). However, our results also show, and confirm, that memory remoteness is not the only factor influencing brain MTL activity, as the phenomenological features of episodic AM retrieval are also crucial for the continuous involvement of MTL-neocortical connectivity over time (see also Moscovitch et al., 2005). For example, we found that remote or recent periods which were richer in phenomenal qualities prompted bilateral hippocampal activation, whereas remote or recent periods which were episodic in terms of specificity and details but with a lower level of re-experiencing and phenomenological features gave rise to left hippocampal activation instead. Further arguments are provided, showing that the various phenomenological attributes of episodic AMs, such as re-experiencing and mental visual imagery (i.e., retrieval strategy used, number of images, field point of view), are predictive of hippocampal involvement (both in activation and correlation studies), chiefly right-sided. Like Piefke et al. (2003), we found that positive emotional attributes predicted bilateral hippocampal activation. In the same vein, we also observed that within-MTL connectivity (hippocampus, parahippocampus and amygdala) and MTL-neocortical connectivity was greater for richly recollected episodic AMs, regardless of their remoteness, in line with the recent study of Nadel, Campbell, et al. (2007) which showed that hippocampal–neocortical activation is not influenced by the passage of time (but by multiple retrievals of AM). Lastly, we demonstrated that recollected factual, spatial and temporal elements of specific AMs (Remember responses justified by the recollection of contextual details) were connected to right-sided hippocampal activity. As far as the correlation studies are concerned, the pivotal role of the right hippocampus can be explained by the fact that we used a special episodic AM task designed to prompt the re-experiencing associated with AM retrieval, as well as by the other AM qualities accompanying this re-experiencing. Our overall results suggest that the bilateral or right hippocampus contributes to the successful retrieval of episodic memories, which is largely dependent upon the richness of the phenomenological and spatiotemporal details that are re-experienced, above and beyond their specificity. Recollection was therefore found to be an important determinant of hippocampal activation in terms of the ability to re-experience events and the other AM qualities associated with re-experiencing, such as detail, emotionality, visual imagery and personal significance, all these features being described as important characteristics of episodic AMs, contributing to autonoetic consciousness.

Finally, the issue of hippocampal laterality in AM remains the subject of much debate. In keeping with our lesion study in epileptic patients, Gilboa et al. (2005), unlike Kopelman et al. (2003), found a significant correlation in patients with AD between remote AM and the amount of remaining tissue in bilateral MTL. This correlation was stronger on the right than on the left, while personal semantic memory was mainly related to a pattern of bilateral anterior and posterior lateral temporal cortex decline, which was more pronounced on the left. We also reported a link between right MTL glucose metabolism in AD patients and recent episodic AMs (unlike semanticized remote AMs). Regarding our activation studies, the results differ from most neuroimaging studies of AM, which have reported the constant involvement of the hippocampus, preferentially left-lateralized like the prefrontal cortex (Maguire, 2001). Some studies have suggested that a more bilateral network may be activated in frontal and medial temporal regions during episodic AM retrieval, depending on the recency of memories (Maguire & Frith, 2003b), as well as the age of the subjects (for a review, see Piefke & Fink, 2005) and the presence of amnesia (Maguire, Vargha-Khadem, & Mishkin, 2001). A reduction in hemispheric asymmetry (see the Hemispheric Asymmetry Reduction in OLDder adults model of ageing effects, Cabeza, 2002) could account for the bilateral involvement of the hippocampus, suggesting in turn the existence of compensatory processes. However, our results are in keeping with recent data revealing that the re-experiencing of recollected memories and the qualities of these memories may influence hippocampal engagement independently of factors such as remoteness and age. For example, some activation studies have detected bilateral or right hippocampal activation when subjects, regardless of their age, become engaged in the retrieval of specific autobiographical memories rated highly in terms of mental imagery, richness of detail, emotionality, reexperiencing or personal significance (Addis, Moscovitch, Crawley, & McAndrews, 2004; Daselaar et al., 2008; Greenberg et al., 2005; Markowitsch et al., 2000; Piefke et al., 2003; Steinvorth, Corkin, & Halgren, 2006). Overall findings suggest that, above and beyond the specificity of memories which may be sustained by the left hippocampus, the phenomenological qualities of memories may activate the bilateral or right hippocampus.

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In summary, the findings of our activation and correlation studies of healthy subjects and our neuropsychological and neuroimaging studies of epileptic patients stress the role of the bilateral or right MTL in the recollection of rich recent and remote episodic AMs. Interestingly, however, they indicate that the Multiple Trace Theory (and more generally models of memory consolidation) could be supplemented and possibly strengthened by a more accurate consideration of the way in which the MTL-neocortical interaction is modulated by the phenomenal features of memories that are retrieved, such as re-experiencing, emotion and self perspective, or frequency of AM retrievals (see Nadel, Winocur, et al., 2007; Nadel, Campbell, et al., 2007). As stressed recently by Moscovitch (2008), the exact role of hippocampus regarding the complex reconstructive processes in episodic memory over the course of time is one of the key challenges of current cognitive neuroscience.

In conclusion, as Tulving (2002) explains, "people can have mental access to their personal past not only in terms of autonoetic remembering but also in terms of nonautonoetic knowing" (p. 7). By developing a paradigm specifically designed to assess the three prerequisites of episodic autobiographical memories – self, autonoetic consciousness and subjectively sensed time – we have shown that knowing develops before remembering in children and that remembering is more susceptible to deterioration over time and with age, as well as in most patients with cerebral lesions, with different profiles corresponding to different situations. Our present data, based on neuropsychological and neuroimaging studies, highlight the importance of the phenomenological self in maintaining a sense of continuity in subjective time, and of the prefrontal lobe in implementing self-related retrieval strategies and hippocampus in re-experiencing the past regardless of its remoteness. At the cognitive and neural level, they also reveal the complexity of the constructive and dynamic nature of episodic AMs over time.

The study of episodic AMs confirms that episodic memory is "really a marvel of nature" (Tulving, 2002, p. 19), and the richness of these episodic AMs will undoubtedly prove particularly useful for honing the concept of episodic memory still further. As Endel Tulving has written, "It took biological evolution a long time to build a time machine in the brain, and it has managed to do it only once, but the consequences have been enormous: by virtue of their mental control over time, human beings now wield powers on Earth that in many ways rival or even exceed those of nature itself. It is difficult to imagine a marvel of nature greater than that." (Tulving, 2002, p. 20). Another vital task will be to continue making the study of AM (and its two components, i.e. episodic memory and semantic memory) a more integral part of models of human memory (Eustache & Desgranges, 2008; Piolino, Desgranges, & Eustache, 2008). Last but not least, it will be particularly rewarding to continue our cognitive and neural exploration of the interactions between autobiographical memory and working memory (Baddeley, 2000), perceptual memory (Gagnepain, Lebreton, Desgranges, & Eustache, 2008), and procedural memory (Beaunieux et al., 2006). A truly exciting prospect indeed!

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