

Underlying mechanisms of episodic autobiographical memory and self-consciousness

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Abstract

Cognitive neuroscience has been examining consciousness associated with the subject, that is the self of the conscious experience and its related multisensory processing of bodily signals, the so-called bodily self-consciousness. Different line of research has highlighted the concept of the autobiographical self in memory and the associated autonoetic consciousness, that is the human ability to mentally travel in time. The subjective re-experiencing of past episodes is often described as re-living them from a viewpoint and location that is similar to the initial encoding. In the first part of my thesis, I have studied how self-relevant bodily cues and personal memories influence our sense of self. In the second part, I have examined how the self is involved in spontaneous thoughts. Through a collection of four studies, I will argue here that it is possible to explore the underlying characteristics of self-consciousness and its relation to bodily signals and memory by a number of cognitive neuroscience approaches, including virtual reality (VR), electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). First, I investigated how the presence or absence of multisensory bodily cues influences long-term episodic autobiographical memory by using immersive VR environment. Second, I examined the underlying brain mechanisms of bodily-self and autobiographical-self by combining a meta-analytical approach with recent fMRI results from (a) patients suffering with out-of-body experiences and (b) healthy participants with induced illusory states of bodily self. Third, I explored how the immersive VR technology can be used to selectively and retroactively strengthen episodic autobiographical memory. Fourth, I examined whether it is possible to capture the inner, self-relevant conscious thoughts and record them with both fMRI and EEG methods. The results from my thesis indicate that (a) the bodily cues fundamentally influence the autobiographical memory and (b) it is possible to manipulate the self-related nature of conscious thoughts. I will discuss my findings with reference to current understanding of bodily-self, autobiographical-self and their links to theories of self-consciousness. Finally, based on my results, I will suggest what should be the following, future step towards memory prosthesis.

Key words: self-consciousness, episodic autobiographical memory, bodily self, first-person perspective, virtual reality, EEG, fMRI

Résumé

Les neurosciences cognitives ont examiné la conscience associée au sujet, c'est-à-dire le soi de l'expérience consciente et son traitement multisensoriel connexe des signaux corporels, appelée la conscience de soi corporelle. Différents axes de recherche ont mis en évidence le concept de soi autobiographique dans la mémoire et la conscience auto-noétique associée, c'est-à-dire la capacité humaine à voyager mentalement dans le temps. La ré-expérience subjective des épisodes passés est souvent décrite comme une revivification à partir d'un point de vue et d'un emplacement similaire à l'encodage initial. Dans la première partie de ma thèse, j'ai étudié l'influence des indices corporels et des souvenirs personnels sur notre identité. Dans la deuxième partie, j'ai examiné comment le soi est impliqué dans les pensées spontanées. À travers un ensemble de quatre études, je soutiendrai ici qu'il est possible d'explorer les caractéristiques sous-jacentes de la conscience de soi et de sa relation avec les signaux corporels et la mémoire par un certain nombre d'approches neuroscientifiques cognitives, notamment la réalité virtuelle (VR), l'électroencéphalographie (EEG) et imagerie par résonance magnétique fonctionnelle (IRMf). Tout d'abord, j'ai étudié l'influence de la présence ou de l'absence d'indices corporels multisensoriels sur la mémoire autobiographique épisodique à long terme en utilisant un environnement immersif en réalité virtuelle. Deuxièmement, j'ai examiné les mécanismes cérébraux sous-jacents du soi corporel et du soi autobiographique en combinant une approche méta-analytique avec les résultats récents d'IRMf de (a) patients souffrant d'expériences hors du corps et (b) de participants sains présentant des états illusoire induits de soi corporel. Troisièmement, j'ai exploré comment la technologie immersive de réalité virtuelle peut être utilisée pour renforcer sélectivement et rétroactivement la mémoire autobiographique épisodique. Quatrièmement, j'ai examiné s'il était possible de capturer les pensées conscientes internes importantes pour l'autosuffisance et de les enregistrer à la fois avec les méthodes IRMf et EEG. Les résultats de ma thèse indiquent que (a) les indices corporels influencent fondamentalement la mémoire autobiographique et (b) il est possible de manipuler la nature liée à soi des pensées conscientes. Je discuterai de mes découvertes en me référant à la compréhension actuelle du soi corporel, du soi autobiographique et de leurs liens avec les théories de la conscience de soi. Enfin, sur la base de mes résultats, je suggérerai quelle devrait être la prochaine étape vers la prothèse de mémoire.

Mots-Clés: conscience de soi, mémoire autobiographique épisodique, moi corporel, perspective à la première personne, réalité virtuelle, EEG, IRMf

In memory of
Prof. PETER G. H. CLARKE (1946-2015)
neuroscientist, mentor and dearly missed friend

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1 Introduction

Consciousness is everything that we subjectively experience, referred to as *qualia*, i.e. the qualitative feeling within an experience (e.g., listening to music or feeling a pain) (Tononi et al., 2016). The conscious experience of self-related events is perceived as embodied, i.e. our physical body is a central object surrounded by a world. We observe the world from an inside view-point of our body (Mach, 1897). Self-consciousness, which defines the self as a subject of conscious experience (Damasio, 1999), originates at different levels from a simple (i.e. *the minimal level of unconscious experience*) to a complex phenomenon (i.e. *the core self* and *the autobiographical self*). Central to episodic autobiographical memory is *autonoetic consciousness*, i.e. the subjective feeling of re-living the past and mentally travelling back in time (Tulving, 1985). In my thesis, I will argue that the underlying aspects of self-consciousness and its relation to memory and body can be studied by using a number of cognitive neuroscience approaches, including virtual reality (VR), electroencephalography (EEG) and functional magnetic resonance (fMRI).

An essential aspect of consciousness is its link with a self, that is the subject of conscious experience. The minimal level of conscious experience, *the core consciousness*, occurs while the brain continuously builds a mental representation of the minimal sense of self, *the core self*, caused by an interaction with internal or external stimuli (Damasio, 1999). The association between the particular body-representation in the brain and the subject of an experience has been investigated neuroscientifically (Ehrsson, 2007; Lenggenhager et al., 2007). Blanke and Metzinger (2009) proposed that a minimal sense of self is centered on the integration of multisensory bodily processing (e.g. vision, touch, proprioception, vestibular and visceral signals) in the brain. We experience the world with an egocentric perspective and from a physical location of the body. “*The body is always there*” as highlighted by William James (1890), the pioneering psychologist and philosopher.

Conscious experience is not always bound to here and now. What did you eat for breakfast yesterday? Where do you have to go today? When is your meeting tomorrow? The human mind is able to detach itself from the present moment and mentally travel to the past or imagine the future. As defined by Damasio (1999), *the autobiographical self* represents a mental state derived from the retrieval of self-relevant memories. No scene captures the human ability to re-experience past event better than the well-known Marcel Proust’s “madeleine moment”. Struggling to remember details of his childhood, Marcel tastes a petite madeleine soaked in

lime-blossom tea “... and suddenly the memory revealed itself. The taste was that of the little piece of madeleine...had recalled nothing to my mind before I tasted it. And all from my cup of tea.” Endel Tulving (1985) associated the subjective possibility to mentally travel in time with auto-noetic consciousness, i.e. the conscious self-experience in the subjective sense of time. The mental time travel relies on episodic autobiographical memory, which allows humans to mentally detach themselves from a current self-location and consciously identify themselves at another particular place and time.

In order to examine the cognitive, behavioral mechanisms operating during self-consciousness, it is essential to better understand the neuronal mechanisms underlying them. “As we take a general view of the wonderful stream of our consciousness, what strikes us first is this different pace of its parts. Like a bird’s life, it seems to be made of an alternation of flights and perchings.” As William James (1890) pointed out, even though self-consciousness seems to be continuous as a stream of water, in fact it is composed of “perchings”, representing brain states with its specific mental contents, and “brief flights”, representing the fast transitions between mental states. Lehmann et al. (1987) suggested that these short-lasting mental states are represented by stable global patterns of electrophysiological brain activity, which they called the “microstates of cognition” or “atoms of thoughts”.

My thesis tries to answer these key questions:

Using VR: What are the fundamental functional and anatomical connections between episodic autobiographical memory and the sense of bodily-self?

Using EEG and fMRI: Can we capture the spatiotemporal dynamics of large-scale brain networks associated with episodic autobiographical memory?

1.1 Self-relevant memories

The relation between the sense of self and episodic autobiographical memory lies at the core of our understanding of consciousness. One's autobiographical memories and sense of self are closely related. The self, i.e. the mental processes that create the subjective feeling that defines us as unique human beings, is a critical component of consciousness (Damasio, 2003). Memory is necessary for everything we do and provides continuity from one moment to another. Memory creates our conscious sense of identity, which we construct based on self-relevant past events. The relation between the sense of self, autobiographical memory and consciousness captivated philosophers and thinkers for centuries (Descartes, 1637; James, 1890; Locke, 1690) and has engaged neuroscientists until this day (Damasio, 1999; Klein, 2016; Prebble et al., 2012; Svoboda, 2009). We are still far from a clear understanding of the underlying mechanisms and associations between consciousness, self and memory. Yet, the story of patient H.M., arguably the most influential case study in the history of neuroscience, answered more questions about memory, self-consciousness and its underlying brain mechanisms than the entire previous century of scientific research.

1.1.1 The role of the self in autobiographical memory

Henry Molaison, patient H.M., became amnesic after his surgery, which involved a bilateral medial temporal lobe (MTL) resection to ease his epilepsy (Scoville and Milner, 1957). Unexpectedly, even though the targeted resection of the MTL structures helped to treat his epilepsy, patient H.M. at the age of 27 lost the ability to form new memories. One of the fundamental characteristics of the normally functioning human brain is its ability to acquire new information from experience and retain it in memory over time (Kandel, 2001). Patient H.M. was left only with his past, particularly the general knowledge that he had acquired before his surgery. It is meaningful to characterize memories by the length of information retention as James (1890) described *"The first point to be noticed is that for a state of mind to survive in memory it must have endured for a certain length of time."* Indeed, the temporal component of memory is one of its essential characteristics (Dudai, 2004). Patient H.M. could not transfer most of the newly acquired information into his long-term memories, however his short-term memory was intact. Remarkably, James (1890) was the first one who theoretically distinguished between two types of memories, which he called primary and secondary memories. James wrote about the primary memory, which is equivalent to the short-term memory, that *"the stream of thought flows on; but most of its segments fall into the bottomless abyss of oblivion. Of some, no memory survives the instant of their passage."* By contrast, secondary memory, which is

equivalent to long-term memory, James defined as “*the knowledge of a former state of mind after it has already once dropped from consciousness; or rather it is the knowledge of an event, or fact, of which meantime we have not been thinking, with the additional consciousness that we have thought or experienced it before.*” The clinical case of patient H.M. confirmed William James’s theoretical assumptions that short- and long-term memories depend on separate cognitive mechanisms. Patient H.M. had to depend on his short-term memory in his everyday life. He was able to speak in fluent sentences and answer any instantaneous questions. However, he could not integrate his current thoughts with his past memories.

Neuroscientists gained new insights from the case H.M., which allowed to classify memories into specific cognitive processes. The long-term memory of patient H.M., especially memory of past self-related episodes was impaired. Yet, he was for example able to draw a spatial map of his house without any conscious recollection of doing so. The pioneering work of Brenda Milner (1962) with patient H.M. lead to the conceptualization of long-term memory into two distinct systems: (a) non-declarative, so-called implicit memory, which does not require conscious awareness in order to learn a new information (e.g., *biking*) and (b) declarative, so-called explicit memory, which relies on the conscious awareness of the acquired knowledge. Declarative memory is further divided into episodic memory, which is accompanied by a subjective feeling of retrieving details of experienced episodes (e.g., “*What did you eat for breakfast this morning?*”) and semantic memory, which consists of general facts (e.g., “*What is the capital of Czech Republic?*”). Patient H.M. was important for the understanding of the types memories that function within and outside of conscious awareness. Patient H.M. could learn implicitly, without using explicit retrieval processes and without consciously recollecting the learning process.

Memories are not static (Dudai et al., 2015). They continuously change with gained experience throughout a person’s life. However, to make the scientific study of memory well-controlled and objectively measurable, cognitive neuroscience researchers further divided declarative memory into discrete stages. This artificial division is an obvious simplification, but a necessary one as it allows to examine and describe any specific details within each form and stage of memory independently. Encoding, consolidation and retrieval are commonly studied using separate experimental designs in the laboratory settings. Yet in real life, memory is a set of dynamic, integrated processes including encoding, consolidation and retrieval, which occur constantly and simultaneously (e.g., an exposure to a familiar stimulus may simultaneously induce memory encoding and retrieval) (Ben-Yakov et al., 2014). Understanding the basic parts

of memory formation is essential to construct these parts into a coherent story. The case of patient H.M. initiated decades of research exploring the behavioral and neural processes within each of the memory stages. The first stage is *encoding*, during which an information is perceived and attended for the first time (**Fig. 1A**). Patient H.M. had no problem encoding information; his deficit was in consolidating, storing and later retrieving facts and events. Memory *consolidation* is a process during which an initial experience is transformed into a long-term memory and re-organized over dispersed brain circuits (Dudai et al., 2015) (**Fig. 1B**). The possibility of memory *retrieval* is a consequence of efficient memory encoding and consolidation. It is the process by which one may access an information from the past event in the present moment in order to re-experience it again (**Fig. 1C**). Patient H.M. could recall information that he had consolidated and stored before his surgery. Yet, he could not integrate the old memory with information from his present life.

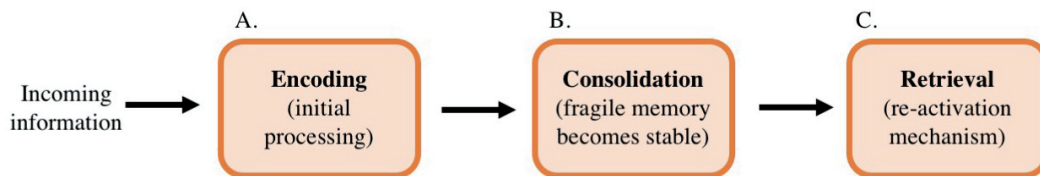


Figure 1. Stages of Memory. **A. Encoding** is the first stage of memory formation. Once we obtain the information from the environment, the information is coded and organized. **B. Consolidation** is the time-dependent process that determines which of the newly encoded experiences will be preserved into long-term memories. During this stage, memory undergoes a storage process that strengthen memory traces over time. **C. Retrieval** is the process of accessing information from our past experiences, bringing them together with our present experiences. Memory retrieval is the process that reflects both encoding and consolidation. During this stage, the qualitative characteristics of memory, e.g. enhancing subjective sense of remembering, may be modified.

1.1.2 Autonoetic Consciousness and Mental Time Travel

In experimental settings, different types and stages of memory have been studied using distinct tasks and measures. Astonishingly, when tested on memory recognition task (i.e. participants are instructed to categorize old and new stimuli) in a laboratory setting, the performance of patient H.M. was impaired after 1 and 3 days, but became similar to healthy control participants after one week (Freed et al., 1987). In more detail, patient H.M. saw 120 complex pictures illustrating nature, people and animals in 4 blocks of 30 pictures each for 20 seconds compared to participants in the control group who saw each picture for 1 second only. The rate of patient H.M.'s forgetting was tested during following recognition task after 10 minutes, 1 day, 3 days and a week. On each recognition trial, he had to choose between 2 pictures and answer the question “*Is this an old or new picture?*”. Patient H.M. had permanently impaired long term

memory, yet surprisingly he showed normal forgetting comparable to healthy controls on this laboratory-based, picture-recognition task (Corkin, 2013). This finding was an exception, which stood in a contrast to other studies, which show that recognition memory is defective after MTL damage (Reed et al., 1997). Thus, there is no doubt that recognition memory is impaired after MTL damage. However, already James (1890) suggested that recognition of stimuli which one has seen before may be constructed by two separable memory processes, the so-called recollection and familiarity: *“I enter a friend’s room and see on the wall a painting. At first I have the strange, wondering consciousness, ‘surely I have seen that before,’ but when or how does not become clear. There only clings to the picture a sort of penumbra of familiarity, - when suddenly I exclaim: “I have it, it is a copy of part of one of the Fra Angelicos in the Florentine Academy - I recollect it there!”* Recent neuroscientific research (Yonelinas and Jacoby, 2012) have provided an experimental support to James’s theoretical assumptions that two distinct memory retrieval processes underlie memory recognition. In one of the first experimental, laboratory-based studies, participants were asked to memorize 60 words (Atkinson and Juola, 1974). In a following recognition test, participants saw one word at a time and had to decide whether they had previously memorized it or not. While recollection reflects a conscious, effortful search for stored memory, familiarity represents a vague feeling of remembering. The surprising results from testing patient H.M. on the lab-based memory recognition task not only confirmed the so-called *dual-process theories* (Jacoby, 1991; Yonelinas, 1994), but also suggested that they are processed by independent brain circuits. The distinction between familiarity and recollection helped the cognitive neuroscientists to understand the ability of patient H.M. to recognize complex pictures up to 6 months after encoding, while he was not able to retrieve anything from his everyday life. When patient H.M. saw pictures of complex scenes, he recognized them based on his sense of familiarity without explicitly recalling having seen them. The declarative memory of patient H.M. was deficient due to the hippocampal lesions, yet he was left with a vague sense of familiarity that helped him to cope with his amnesia.

Although the number of experiments with self-related, personal stimuli has increased (Cabeza et al., 2004; Schacter et al., 2011; Vogel and Schwabe, 2016), the use of personally-irrelevant, laboratory-based stimuli is still one of the most widely used methods in studying episodic memory. Importantly, the examination of patient H.M. revealed that even though he was able to perform well on classical, laboratory-based memory recognition tasks, his memory deficits were specific to autobiographical memory. In more detail, Corkin (1984) selected 36 self-relevant photographs from patient H.M.’s childhood and the same number of unrelated-family

photographs were selected to test his autobiographical memory. Interestingly, patient H.M. was able to correctly recognize his family members, yet his performance showed that he answered differently from healthy participants. When asked about family vacation, most of us can recall vivid moments with multisensory details, including smells, sounds, and sensory description. Patient H.M. constructed his responses primarily on the general, semantic autobiographical knowledge about his family, but he could not consciously re-live any of the past events. Tulving (1972) theoretically distinguished the declarative memory into episodic (**Fig. 2A**) and semantic (**Fig. 2B**) memories based on their distinct states of consciousness.

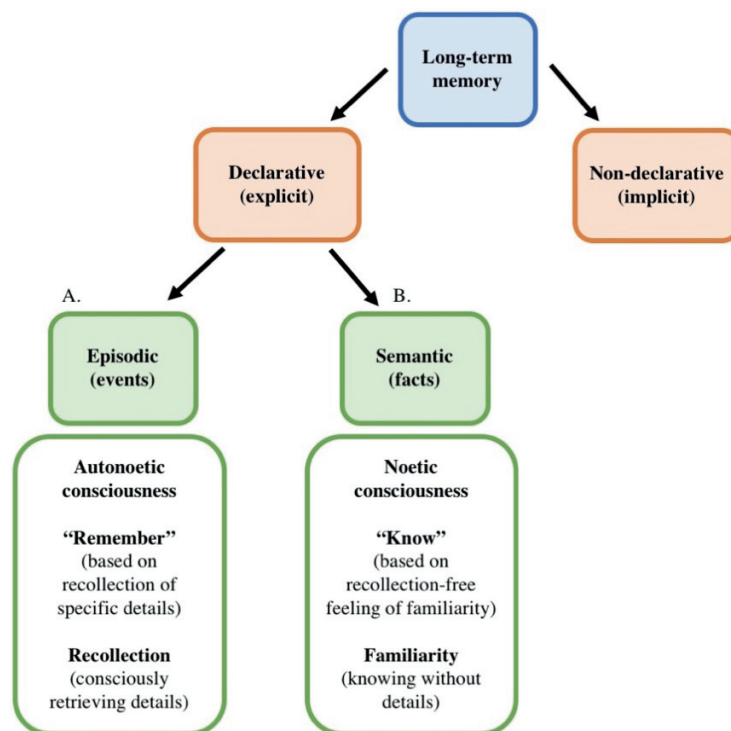


Figure 2. Declarative memory sub-systems based on distinct states of consciousness. Declarative, explicit memory contains two sub-groups: **A. Episodic memory**, which is accompanied by a subjective feeling of retrieving personally experienced episodes and **B. Semantic memory**, which consists of facts and general knowledge. It is possible to distinguish declarative memory based on distinct states of consciousness. **Autonoetic consciousness** (self-engagement in the memory accompanied by contextual details “what”, “where”, “when”, how”) underlies episodic memory and **noetic consciousness** (without details of the encoded episode) is associated with semantic memory. Furthermore, **remembering** is related to specific details of episodic memory, while **knowing** is without specific recollection of the past episode. **Recollection** is a conscious, effortful search for stored memory associated with rich, vivid memories, while **familiarity** represents the vague feeling of knowing.

Autonoetic consciousness characterizes episodic memory, which allows one to know what happened in the past and remember specific past events. In fact, it requires to move from the representation of past experiences to self-engagement in the experiences. To mentally travel in time to meaningfully connect the past self with the present self is the core of episodic

autobiographical memory. *Noetic consciousness* characterizes semantic memory which underlies an explicit knowledge about the world, general concepts and facts. Based on the theoretical distinction between auto-noetic vs. noetic consciousness, Tulving (1985) developed an experimental *remember/know paradigm*. This paradigm relies on participants' reports regarding their subjective state of awareness during memory retrieval tasks. *Remembering* has been related to the episodic autobiographical memory (i.e. stimuli evoke a specific memory for the episodic setting in which they were experienced), while the semantic autobiographical memory is accompanied by the sense of *knowing* (i.e. the stimuli is experienced without a specific recollection of a past episode). Tulving's classification of declarative memory into episodic and semantic is the basis on which to differentiate between recollection and familiarity.

1.1.3 Parietal regions and the subjective experience of remembering

Numerous fMRI studies investigated the episodic memory and identified the core memory network, comprising enlarged activity primarily in the hippocampus, the medial prefrontal cortex and the angular gyrus (Levine et al., 2004; Schacter et al., 2012; Svoboda et al., 2006). These neural components of episodic memory are crucial in order to retrieve the conscious past experiences and any damage to this network may have fundamental consequences to everyday life (Scoville and Milner, 1957; Steinworth et al., 2005). Since the discovery of patient H.M.'s amnesia due to MTL damage (Scoville and Milner, 1957), neuroscientists have investigated the critical role of these brain structures in contributing to conscious memories. Examining the effects of brain lesion on mental functions revealed that particular brain regions are necessary for distinct cognitive functions. Recently, studies investigating memory in patients with lateral parietal lesions (Ben-Zvi et al., 2015; Berryhill et al., 2007; Levy, 2012; Simons et al., 2010) suggest that the ventral posterior parietal cortex (specifically, the angular gyrus and the temporoparietal junction) shows an increased activity for retrieval of episodic autobiographical memory associated with rich and vivid episodic details (i.e. recollection). Although lateral parietal lesion patients can successfully retrieve episodic memories, the vividness and confidence in the self-related memories is weakened (Berryhill et al., 2007; Simons et al., 2010). These results imply that the angular gyrus of the parietal lobe plays a key role in the subjective experience of retrieving multisensory episodic autobiographical memory (Moscovitch et al., 2016; Simons et al., 2010) (**Fig. 3**).

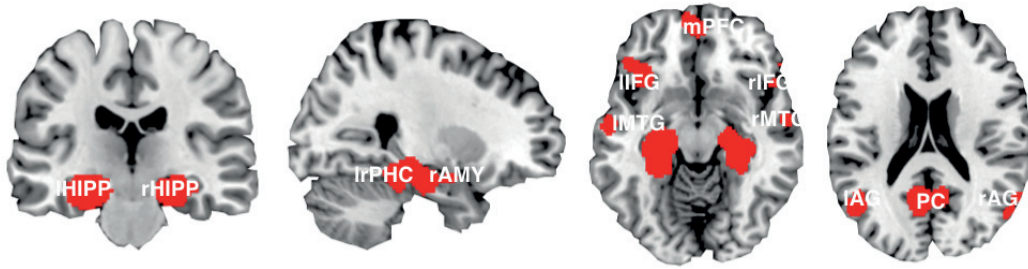


Figure 3. Episodic Autobiographical Memory Network. The quantitative activation likelihood (ALE) meta-analysis (Eickhoff et al., 2009, 2012; Turkeltaub et al., 2012) of 41 episodic autobiographical memory studies showed bilateral activations in the angular gyrus and the left superior temporal gyrus. Activations were found in cortical midline structures, i.e. bilaterally in the posterior cingulate cortex and left anterior cingulate cortex. The analysis also revealed activity bilaterally in the hippocampi and adjacent parahippocampal gyri and in the left inferior temporal gyrus. Other clusters were found in the left inferior frontal gyrus, bilaterally in superior frontal gyrus and in the left middle frontal gyrus (for more details see Study 2).

1.2 Bodily Self Consciousness

A key feature of consciousness is its relation with a self as the subject of conscious experience (Blanke, 2012). Cognitive neuroscientists have established a link between a particular body representation in the brain and the subject of an experience. The inner aspect of the functional state of human brain is the subjective, first-person experience of consciousness. We experience the world with an egocentric, first-person perspective (1PP) of the physical body, which we feel as our own (Blanke, 2012; Blanke et al., 2015; Mach, 1897). Neuroscience-based investigations of self-consciousness emphasized that *the sense of embodiment/bodily self-consciousness* essentially relies on the accurate integration of body-related, multimodal information (e.g. vision, touch, proprioception, vestibular and visceral signals) and *the sense of agency*, i.e. the subjective experience of being responsible for one's own actions. Blanke and Metzinger (2009) identified three fundamental aspects of the bodily self-consciousness: a. *self-identification/body ownership* (i.e. the experience of owning a body), b. *self-location* (i.e. the experience of being a physical body in a given location) and c. *first person perspective* (i.e. perspective on the environment).

1.2.1 Experimental illusory states of bodily self

The multisensory brain mechanisms that underlie the integration of bodily signals, the so-called *bodily self-consciousness*, create the subjective feeling of being a subject of a conscious experience (Blanke et al., 2015). Experimental studies on multisensory bodily processing, which investigate the subject (or "I") of experience, have previously stimulated *illusory states* of bodily self-consciousness. An illusory sensation of ownership, i.e. the feeling of owning a

body part, can be induced by visuo-tactile manipulations on one's own and an artificial hand, the so-called *rubber hand illusion* (Botvinick and Cohen, 1998). During the experiment, participants are instructed to observe a rubber hand, while their own hand is out of sight. When both their own, hidden hand and the visible, rubber hand are stroked in synchrony, participants report a subjective feeling as if the rubber hand would be their own hand (**Fig. 4A**). During this experimental manipulation, the vision of the rubber hand becomes dominant over the proprioceptive (i.e. information about the real position of one's own body in space) signals and as such results in *the self-attribution* of the rubber hand. The effect of the rubber hand illusion is most often measured with questionnaires or the proprioceptive drift (i.e. the mislocation of the stroked hand towards the rubber hand) (**Fig. 4B**).

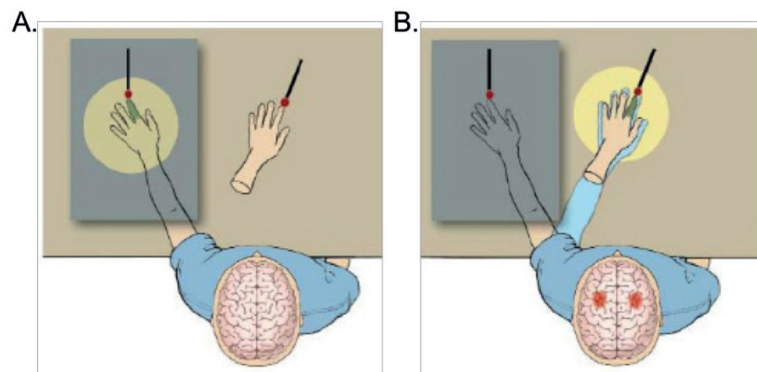


Figure 4. The Rubber Hand Illusion. **A.** Participant's left hand is out of sight and instead, the rubber hand is visible. The hidden own hand as well as the visible rubber hand of the participant are touched in synchrony. **B.** The synchronous visuo-tactile stimulation creates a subjective feeling that the rubber hand belongs to participant's body as measured with questionnaires and the proprioceptive drift. Figure from Botvinick and Cohen (1998).

The rubber hand illusion allows the examination not only of the multisensory integration of vision, touch and proprioception, but also the perception of our bodily self and body ownership. The recent development of robotics and virtual reality enable to experimentally study the bodily self as unitary entity. *The full body illusions* examine the behavioral and neuronal mechanisms beyond the ownership of body parts. In the experimental paradigm of Lenggenhager et al. (2007), participants saw their own virtual bodies 2 meters in front of them filmed and shown through a head mounted-display, while being stroked on their back (**Fig. 5A**). In temporally synchronous conditions between the seen and felt stroking (i.e. visuo-tactile synchrony), participants perceived the virtual body as their own (i.e. change in *self-identification*) and felt as if they were displaced towards the virtual body (i.e. change in *self-location*). Participants were then instructed to respond to questions about the state of their self-identification (Q1: *How strong was the feeling that the body you saw was you?*), illusory touch (Q2: *How strong was*

the feeling that the touch you felt was located where you saw the stroking?), self-location (Q3: *I felt as if my body was drifting toward the virtual body*), and control question (Q4: *I felt my body as usual, nothing changed*) using a 7-point scale. Additionally, the changes in self-location were measured by blind-folding participants, relocating them after inducing the full body illusion and requesting them to return to the original location.

Similarly, Ionta et al. (2011) applied synchronous tactile stimulation on the backs of participants when they were lying in the MRI scanner. Participants saw a full body figure stroked on its back congruently or incongruently with stroking of participants' own back. The synchronous visuo-tactile stimulation induced higher self-identification towards the virtual body, as compared to the asynchronous condition. Interestingly, in this study, even though all of the participants were lying on their backs in the scanner, half of the participants experienced looking upward at their virtual body (i.e. “up-looking group”, 1PP) (**Fig. 5B**), while the other half of the participants had the feeling of looking down on the virtual body (i.e. “down-looking group”, 1PP) (**Fig. 5C**). Crucially, changes in 1PP were related to changes in self-location, i.e. up-looking participants experienced initially lower position of the self-location and a rise when stroked synchronously, while the down-looking participants experienced a downward drift associated with their self-location. The classical *mental ball dropping task* provided quantifiable measure of self-location, while the participants were lying in the scanner. During this task, participants were instructed to imagine holding a ball and guess how long it would take before the ball would touch the floor.

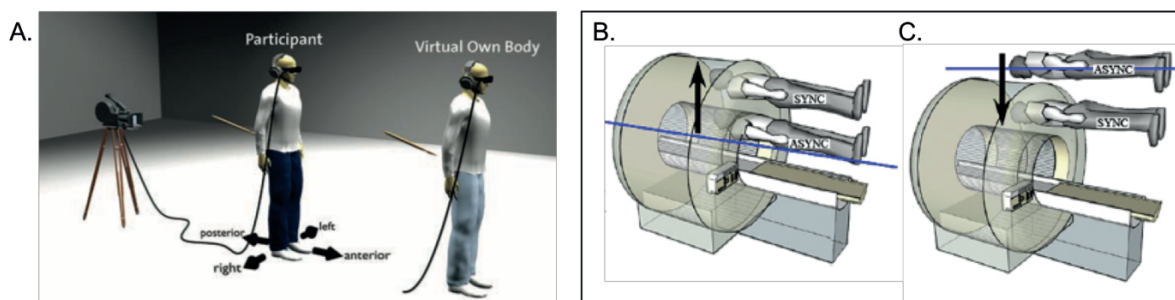


Figure 5. The Full Body Illusion. A. The VR experimental setting of testing bodily-self using the full body illusion paradigm. Figure from Lenggenhager et al. (2007). Participants observe their own back with a head-mounted (HMD) display filmed from cameras located two meters behind them, while the experimenter applies synchronous or asynchronous stroking on the participant's back. **B. Self-location changes** were related to the experienced direction of 1PP: **the up-looking group** of participants experienced an elevation from an initially low self-location when stroked synchronously. **C. The down-looking group** experienced a downward drift. Figure from Ionta et al. (2011).

1.2.2 Neurologically altered states of bodily self

The self is usually experienced as a whole, located in a physical body. However, the bodily self-consciousness, particularly the *self-identification*, *self-location* and *first-person perspective*, may be altered in patients suffering from particular neurological conditions (Critchley, 1950). Altered states of bodily self-consciousness depend on the disintegration of multisensory (e.g., visual, proprioceptive, and somatosensory) bodily signals. These illusory own body perceptions, the so-called *autoscopic phenomena*, comprise autoscopic hallucination, heautoscopy and out-of-body experiences. Patients suffering from autoscopic hallucinations observe their own body in an extra-personal space, but they perceive themselves to be located in their physical body (Fig. 6A). Thus, their sense of location and first-person perspective (1PP) remains intact. Patients suffering with heautoscopy observe their own body in an extra personal space and the subjective sense of self-location shifts between their physical body and their double (Fig. 6B). Patients suffering with out-of-body experiences subjectively feel as if they are out of their physical body, which they observe from an elevated, third person perspective (3PP) (Fig. 6C).

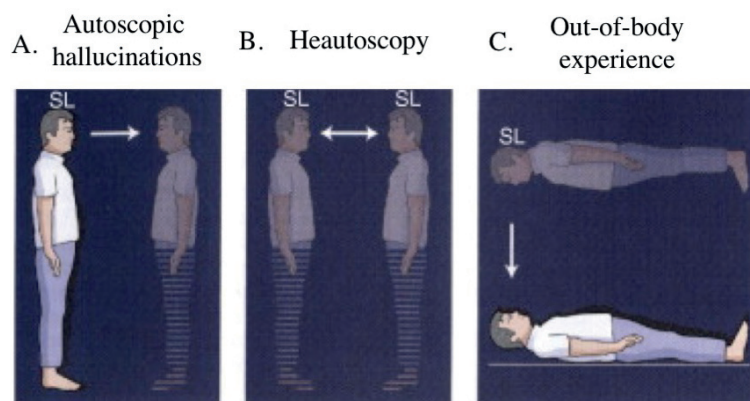


Figure 6. Autoscopic phenomena model. **A. Autoscopic hallucination** patients observe their own body in an extra-personal space, but they perceive themselves to be located in their physical body (1PP). **B. Heautoscopy** suffering patients observe their own body in an extra personal space and the subjective sense of self-location shifts between their physical body and their double. **C.** Patients with **out-of-body experience** subjectively feel out of their own body, which they observe from an elevated, third person perspective (3PP). Figure from Blanke and Metzinger (2009).

Interestingly, Conway et al. (2004) described case studies of patients suffering with posttraumatic stress disorder, who experienced intense intrusion of vividly recollected episodic autobiographical memories of traumatic experiences, which are often associated with changes in perspective. For example, an eye-witness to the terroristic 9/11 attacks consequently suffered with distorted flashbacks in which she saw herself (3PP) flying above the ground and observing the collision of the plane with the building. After several psychotherapeutic sessions, the eye-

witness restored her original perspective (1PP). Functionally, out-of-body experiences are caused by abnormal integration of tactile, proprioceptive, visual and vestibular inputs (Blanke, 2012; Pfeiffer et al., 2014). These altered states of bodily-self have directly motivated the development of experimental paradigms involving VR technology to test the bodily-self states in healthy participants.

1.2.3 Parietal contributions to the self-location and first-person perspective

A number of brain regions become activated during manipulations of bodily self-consciousness, including *the hand ownership*, *the face ownership*, *self-identification* or *self-location* (**Fig. 7**). An enhanced activity in the premotor cortex and intraparietal sulcus is related to the hand ownership or a hand embodiment (Graziano, 1999; Makin et al., 2008), while the activity in the ventral intraparietal area is associated with face-related changes in bodily-self (Apps et al., 2015). The major brain areas associated with self-identification are within the premotor cortex-intraparietal sulcus network, while important regions for self-location are situated in lateral temporo-parietal regions, including supramarginal gyrus, superior temporal gyrus and posterior insula and posterior cingulate cortex (Ionta et al., 2011, 2014; Guterstam et al., 2015). Temporoparietal junction activity reflected changes in self-location and first-person perspective, which were well-matched with clinical data (Blanke et al., 2002; De Ridder et al., 2007; Heydrich and Blanke, 2013). Patients with brain damage in this region suffer from out-of-body experiences. It is also possible to experimentally induce such experiences in epileptic patients by applying 2-seconds electrical stimulation at the right angular gyrus and the superior temporal gyrus (Blanke et al., 2002). Anatomically, out-of-body experiences are the outcome of electrical brain stimulation or brain damage particularly related to the right angular gyrus.

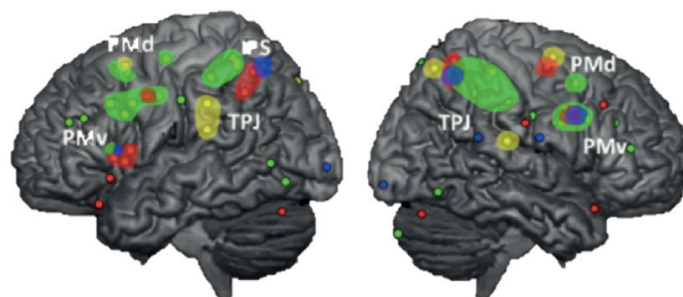


Figure 7. Brain areas associated with manipulations of bodily self-consciousness. Areas are associated with ownership for the hand (in red color: ventral and dorsal premotor cortex, PMv and PMd and intraparietal sulcus, IPS) or face (in blue color: ventral intraparietal area/intraparietal sulcus, VIP/IPS), self-identification (in green color: ventral and dorsal premotor cortex, PMv and PMd and intraparietal sulcus, IPS), or self-location (in yellow color: temporoparietal junction, TPJ). Figure from Blanke et al. (2015).

1.3 Self-generated thoughts

Inspired by Tulving's memory studies (1985, 2002) on mental time travel and mental states of consciousness, neuroscience research embraced the tremendous attention paid to the resting brain's activity and dramatically changed our view on mind-wandering (Christoff et al., 2016; Fox et al., 2015; Smallwood and Schooler, 2015). James (1890) pictured the wandering mind as "*a bird's life consisting of brief flights and perchings*". On a neurological level, the brain is organized intrinsically into widespread networks, each playing an important role in our daily life activities. For example, the so-called default mode network purposefully engages many cognitive processes, enabling our minds to wander during rest (Christoff et al., 2016; Dixon et al., 2018; Spreng et al., 2009). In contrast, when we pay attention to an external event or carry out a specific task, other relevant regions of the brain become active (Christoff et al., 2009; Dixon et al., 2014; Stawarczyk et al., 2017). Sometimes the mind moves spontaneously from one thought to another, however at other times it keeps coming back to the same thought, drawn by a particular past event or an emotional experience. While a healthy person can easily balance time of rest with time of focused attention, someone suffering with a mental health issue may continue thinking about negative past episodes (Smallwood and Andrews-Hanna, 2013). To capture the stream of ongoing internal experiences is challenging, yet important in order to better comprehend the composition of healthy and pathological thoughts.

1.3.1 The conscious experience of the self during rest

Numerous neuroimaging studies have explored spontaneous neural fluctuations of ongoing brain dynamics occurring during rest, i.e. without any explicit task (Biswal et al., 1997; Damoiseaux et al., 2006; Fox and Raichle, 2007; Power et al., 2014). Resting-state functional connectivity explores the neural activity of functionally connected, yet anatomically distant regions of the brain during rest, i.e. the resting-state networks. Most of the studies have explored the link between resting state connectivity patterns and cognition in particular resting state networks, mainly in the default mode network (Buckner, 2012; Raichle, 2015). The default mode network was first described as de-activated during cognitive tasks (Raichle et al., 2001; Shulman et al., 1997). Nonetheless, many studies on cognitive mentation showed that in contrast to other resting state networks, the default mode network shows an increased activity during rest than during cognitive tasks. Internal mental processes that activate the default mode network have been related to the self-referential processes, memory retrieval processes, decision making, theory of mind and prospection (Kim, 2012, 2016; Spreng et al., 2009).

Furthermore, this network also activates when our mind begins to wander (Andrews-Hanna et al., 2014; Kucyi, 2017; Kucyi and Davis, 2014). The study of Andrews-Hanna et al. (2010) showed that the default mode network includes two sub-networks: i.) the *dorsomedial prefrontal cortex subsystem* supports internally-guided cognition and includes the dorsomedial prefrontal cortex, the temporoparietal junction, the lateral temporal cortex and temporal poles. ii.) the *medial temporal lobe subsystem* enables formation of imagined scenes and includes the ventromedial prefrontal cortex, the posterior inferior parietal lobule, the retrosplenial cortex, the parahippocampal cortex and the hippocampus. The anterior medial prefrontal cortex and posterior cingulate cortex represent hubs within the complex network. Several other studies confirmed that the default mode network does not present a unified network, but comprises distinct sub-systems that cooperate over hubs (Andrews-Hanna et al., 2010; Axelrod et al., 2017; Kim, 2012) (**Fig. 8**).

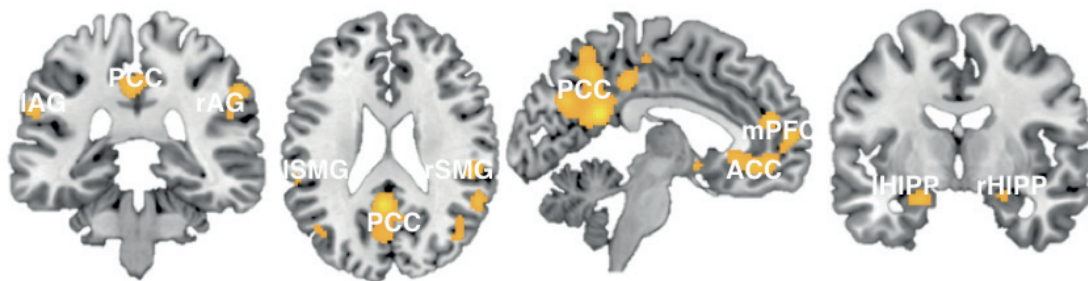


Figure 8. The main brain areas related to the default mode network. The quantitative activation likelihood (ALE) meta-analysis (Eickhoff et al., 2009, 2012; Turkeltaub et al., 2012) of 136 DMN studies showed activity in the cortical midline structures. More precisely, activity was found bilaterally in the ventral and dorsal parts of the posterior cingulate and bilaterally in the dorsal part of the anterior cingulate cortex. Activations were found in the limbic structures, i.e. bilaterally in the parahippocampal gyrus. Furthermore, a cluster was found in the supramarginal gyrus (Bréchet et al., unpublished results).

1.3.2 Methods: fMRI resting states and cognitive task states

Among the most often used functional connectivity techniques belongs the seed-based analysis, which extracts the time-course of the blood oxygen level-dependent (BOLD) signal from a predefined region of interest (ROI) and then identifies regions showing a significant correlation with that specific ROI (Arfanakis et al., 2000; Biswal et al., 1997). This time-course correlation analysis presents a hypothesis driven method, relying on an a priori defined ROI, i.e. the seed. In contrast to the model-dependent methods, the independent-component analysis (ICA) is a hypothesis-free technique examining multiple whole-brain connectivity patterns (Damoiseaux et al., 2006; Smith et al., 2009). ICA decomposes a number of spatial maps, i.e. independent components, from the BOLD signals. Each component presumably represents a common

network of neural or physiological activity. Thus, ICA examines functional resting-state, whole-brain patterns.

Spatial patterns of temporally correlated BOLD signals under resting conditions resemble several brain networks studied during active tasks (Bolt et al., 2017; Cole et al., 2013; Damoiseaux et al., 2006; Mill et al., 2017; Smith et al., 2009). These links between resting states of the brain and specific functional cognitive processes spark a wide attention on the nature of spontaneous activity (Campbell and Schacter, 2017; Davis et al., 2017; Spreng, 2012). Striking similarities have been discovered when comparing the spatial distributions of networks initiated by experimental tasks and those related to self-reported thoughts (Andrews-Hanna et al., 2010b; Axelrod et al., 2017; Shirer et al., 2012), generating a discussion about the mental activity at rest and its content (Bressler and Menon, 2010; Buckner, 2012; Christoff et al., 2016; Davis et al., 2017; Fox and Raichle, 2007; Kucyi et al., 2016; Power et al., 2011; Raichle, 2015; Spreng and Schacter, 2012).

For example, Smith and colleagues (2009) explored the extent to which resting state “functional networks” correspond to functional networks active during explicit cognitive tasks. They hypothesized that a meaningful interpretation across many functional brain networks could be made by directly comparing co-activation networks and resting-state networks. As such, this study independently applied independent component analysis (ICA) to two different data sets. First, to resting state fMRI study of 36 subjects, second to a large database of task-active neuroimaging studies. They expected to find a set of functional networks as seen in resting state data that would closely match a set of task activation studies. This study indicated that the main task-based functional networks appeared to have similar organization as spontaneous resting state co-activation networks, such as executive control network, frontoparietal network, visual network or default mode network (**Fig. 9**). The key finding of this study implied that the intrinsic patterns of the resting brain may be disentangled to reveal task-based, function networks.

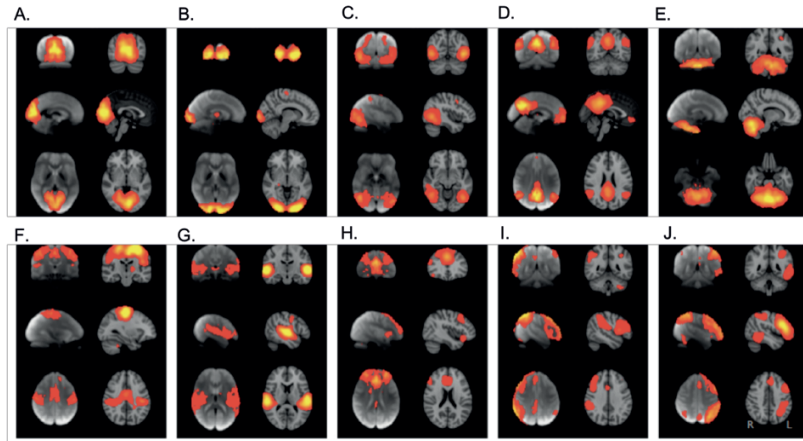


Figure 9. The resting state networks (left) versus large scale cognitive task networks (right). 10 pairs of networks from 20-component ICA of rs-fcMRI (left) and functional BrainMap database (right). **Maps A, B, C** were assigned to the visual network. **Map D** was assigned to the default mode network, **Map E** corresponded to cerebellum, **Map F** corresponded to the sensorimotor network, **Map G** corresponded to the auditory network, **Map H** corresponded to the executive control network, **Map I** and **Map J** were assigned to the fronto-parietal network. Figure from Smith et al. (2009).

Recently, two review articles by Campbell and Schacter (2017) and Davis et al. (2017) pointed to several issues regarding the explanation of resting-states. They reasoned that the extensive use of resting state networks in cognitive neuroscience is based on the idea that resting state networks define cognitive large-scale networks. However, the authors pointed out several problems with this assumption: i.) *regions within a resting state network are often disconnected in different cognitive functional networks*. For example, the brain regions within the default mode network (Andrews-Hanna et al., 2010), such as ACC or PCC, are often disconnected in cognitive tasks (Sestieri et al., 2011a). Therefore, knowing that brain regions are part of the same resting state network does not imply that these two brain regions will also be co-activated during a particular cognitive task. ii.) *regions disconnected in a resting state network become connected in cognitive functional networks*. For example, the prefrontal cortex is typically part of the language network (Lee, 2012) and the hippocampus is classified as part of the default mode network (Kim, 2011). However, these two regions become connected during memory encoding tasks. Therefore, the functional association between regions during a task is often more specific than during rest. iii.) *a particular region within resting state network may have multiple roles in distinct cognitive functional networks*. For example, the ventral parietal cortex is involved in attentional re-orientation, number processing, theory of mind and episodic memory retrieval (Cabeza et al., 2008; Sestieri et al., 2011b). Depending on the functional processes involved, brain regions can rapidly change patterns of functional connectivity. Therefore, resting states cannot explain the fast modifications in patterns of functional connectivity. iv.) *the function of a region cannot be based on its role during rest, because it varies depending on its performance*. For example, the core hubs of the default mode network,

i.e. anterior cingulate cortex and posterior cingulate cortex, become less active during episodic memory retrieval tasks (Rugg and Vilberg, 2013). Thus, the reviews by Campbell and Schacter (2017) and Davis et al. (2017) question whether resting brain activity can truly explain task-based, functional large-scale cognitive networks. The authors argue that to achieve better understanding of the fundamental anatomical and cognitive functions, the resting state studies have to be accompanied by task-based studies.

1.3.3 Methods: Spontaneous EEG microstates

Both conscious thoughts and recall of past events occur in milliseconds (Bressler, 1995; de Pasquale et al., 2017; Koch et al., 2016; Tononi et al., 2016). The dynamics that underlie these subjective experiences have to describe the brain functioning in this brief time range. EEG measures the brain's electrical activity with high temporal resolution (i.e. on the scale of milliseconds) and therefore might be used to investigate the temporal dynamics of mental states (Michel and Koenig, 2018). Lehmann and colleagues (1987) proposed that the spatial and temporal characteristics of resting state networks may be investigated using EEG microstate analysis. *EEG microstates* are defined as global patterns of scalp potential topographies recorded with multichannel EEG that dynamically change over time in an organized pattern (Michel and Koenig, 2018). More specifically, the brain electric activity can be measured on the head surface as potential fluctuations (**Fig. 10A**). To improve the signal to noise ratio (SNR), only the time points of the local maxima of the global field power (GFP), corresponding to high global neuronal synchronization, are used for further analysis (**Fig. 10B**). The broad-band spontaneous activity is then plotted as potential topographies, the so-called EEG maps, at any moment in time (**Fig. 10C**). The temporal sequence of topographical maps appears to be disorganized, however Lehmann et al. (1987) observed that the spontaneous EEG activity, described as scalp potential topographies stays constant for a short time, before transitioning to another topography. Pascual-Marqui et al. (1995) suggested a statistical investigation of the EEG maps' topographies. This data-driven analytical approach is based on *k*-mean cluster analysis (**Fig. 10D**) that groups the EEG topographies with high spatial correlation and defines the descriptive topography. The cluster analysis is first calculated on the individual level, and second on the group level across participants. Surprisingly, only a few cluster maps explain a large portion of the variance of the data. Several studies that used *k*-mean cluster analysis revealed that the optimal number of clusters is 4, explaining about 65% - 85% of the global variance (Britz et al., 2010; Brodbeck et al., 2012). Koenig et al. (1999) initially labelled these 4 maps as class A, B, C and D (**Fig. 10E**). After determining the cluster maps, the temporal

characteristics of microstates can be retrieved. This is achieved by computing spatial correlations between microstate maps identified at the group level and the map at each time point of each participant's EEG. The back-fitting procedure quantifies a number of microstates' parameters, such as *duration* (i.e. the average time a microstate was present) or *the occurrence* (i.e. how often a microstate re-occurred per second).

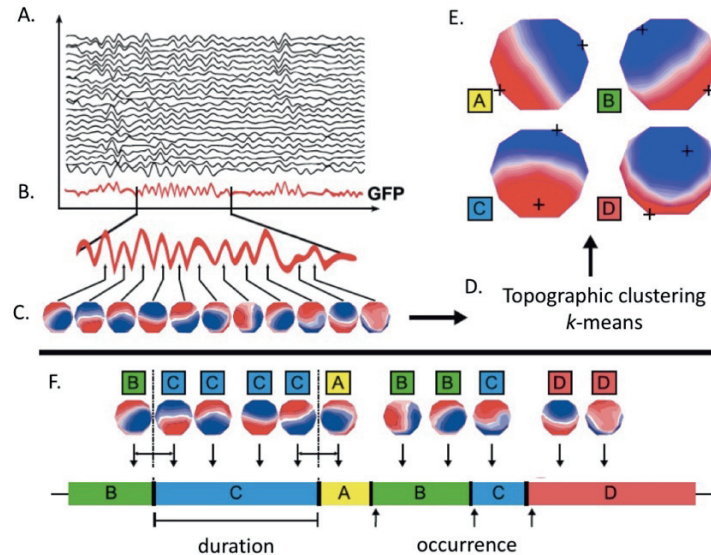


Figure 10. EEG microstate analysis. A. broad-band, spontaneous EEG recording B. The red line indicates the peaks of the global field power (GFP) C. the GFP peaks are presented as topographical maps D. topographical clustering, such as *k*-means clustering E. the group *k*-mean clustering showed 4 dominant EEG microstate topographies F. the EEG recording was characterized at each moment in time by the particular microstate which showed the best correlation. Based on the labelling, the microstate parameters were calculated: microstate duration and occurrence for each participant. Figure from Khanna et al. (2014).

1.3.4 Approaches to measure spontaneous thoughts

The occurrence of spontaneous, personal and inner thoughts presents a unique experimental challenge due to the unconstrained cognitive control (Christoff, 2012; Fox et al., 2015; Kucyi, 2017). fMRI or EEG studies usually relate brain activity during rest to cognitive processes indirectly with questionnaires (Andrews-Hanna et al., 2010a) or by probing participants about their current thoughts during rest (Kucyi et al., 2016; Perogamvros et al., 2017; Smallwood and Schooler, 2015; Stawarczyk et al., 2011). For example, Lehmann et al. (1998) tried to relate EEG microstate to the ongoing mental activity. During this mind wandering study, EEG was recorded from 13 healthy participants at rest. Whenever the participants heard a signal, they were instructed to briefly report “*what just went through their mind*”. About 30 stimuli were given to each participants at random intervals during the continuous EEG recording. The self-reports were audio recorded and independent raters classified the ongoing thoughts of participants as either visual-concrete thoughts (e.g., “*I saw our lunch*”) or abstract thoughts (“*I*

thought about the meaning of a word’’). EEG microstate analysis determined significant topographical differences, specifically between the two classes of thoughts, that is abstract or concrete, in a time-dependent manner of two seconds before the prompt (**Fig. 11**).

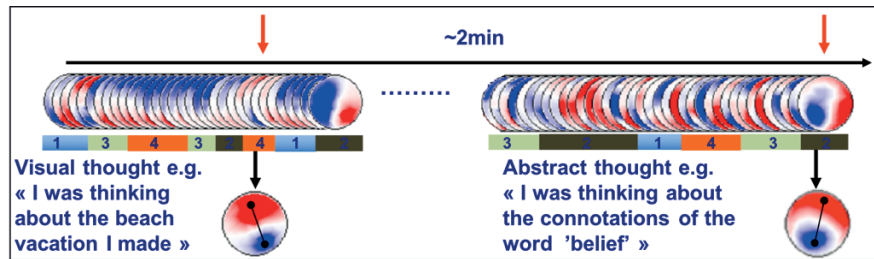


Figure 11. Self-reports of ongoing thoughts with EEG microstates. 30 reports of conscious experiences were collected during rest and categorized into visual imagery and abstract thought. Brain electric activity was uninterruptedly recorded and segmented into microstates. Two types of reported experiences (i.e. visual and abstract thoughts) were related to significant changes in duration and occurrence of two microstates. Figure with courtesy of C. Michel.

Similarly, the fMRI study of Christoff et al. (2009) also used an experience sampling method, which involved irregularly probing participants to specify their current mental state and as such allowing an evaluation of brief changes in the content of consciousness. (**Fig. 12**). Interestingly, the authors report a simultaneous activity in default mode network and executive network *at the same time* during mind-wandering and the activity was the greatest when participants were unaware of mind wandering, i.e. lacking on meta-awareness (i.e. the mental state that arises when explicitly noticing the present content of consciousness) (Smallwood and Schooler, 2015).

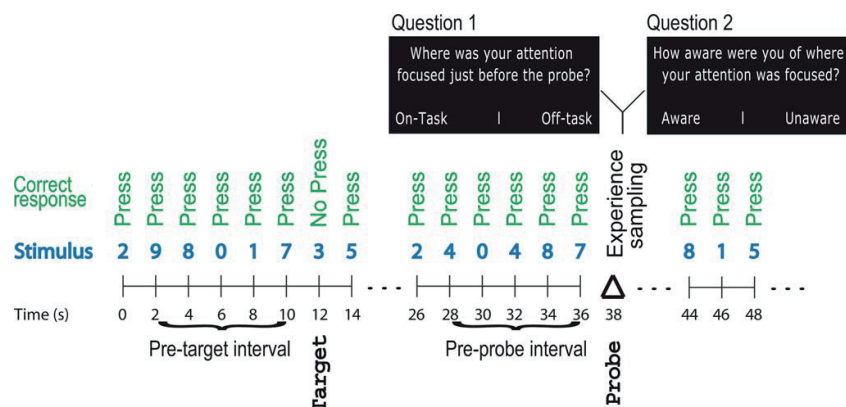


Figure 12. Experience sampling during fMRI recordings. Participants received probes, while performing a go/no-go task. Participants were then asked 2 questions about their current mental state. First question: “Where was your attention focused just before the probe?” Second question: “How aware were you of where your attention was focused?”. Figure from Christoff et al. (2009).

1.4 Thesis outline

The aims of this chapter is to give a short summary of the scientific articles included in the thesis and briefly provide the main motivation, research question, methodology and findings of each publication. The results are then further discussed and integrated in the Discussion section.

- **Bréchet, L.,** Mange, R., Herbelin, B., Gauthier, B., Serino, A., Blanke, O. (2018). Viewing one's body during encoding boosts episodic memory. Under review after 1st revision in *PlosOne*. Preprint published in: bioRxiv, doi: <https://doi.org/10.1101/318956>.
- **Bréchet, L.,** Grivaz, P., Gauthier, B., Blanke, O. (2018). Common recruitment of angular gyrus in episodic autobiographical memory and bodily self-consciousness. In press in *Frontiers in Behavioral Neurosciences*. Preprint published in: bioRxiv, doi: <https://www.biorxiv.org/content/early/2018/06/14/345991>.
- **Bréchet, L.,** Hausmann, S., Mange, R., Blanke, O., Serino, A. The Bodily Self Selectively and Retroactively Strengthens Episodic Autobiographical Memories During Post-Encoding Consolidation. (*in preparation*)
- **Bréchet, L.,** Brunet, D., Birot, G., Gruetter, R., Michel, CM, Jorge, J. (2018). Capturing the spatiotemporal dynamics of task-initiated thoughts with EEG and fMRI. Under review in *Neuroimage*. Preprint published in: bioRxiv, doi: <https://www.biorxiv.org/content/early/2018/06/14/346346>.

1.4.1 Viewing one's body during encoding enhances episodic memory (study 1)

Episodic autobiographical memory studies have been recently conducted using new approaches to (1) control for the stage of memory encoding and (2) reflect a real life-like testing outside the laboratory setting. For example, St. Jacques and Schacter (2013) developed a *museum paradigm*, in which participants encoded episodes while wearing a camera that automatically took photos. Still, these studies did not integrate participants' physical bodies when re-testing the autobiographical memory of the past events. Perceiving one's own physical body as part of a visual scene, such as seeing one's own hand pointing at a painting during a museum tour, relies on a multisensory integration of proprioceptive, visual and tactile cues (Blanke et al., 2015). Subjective experiences create a link between episodic autobiographical memory and bodily self-consciousness, which suggests that the multisensory bodily signals may also be relevant to the conscious re-experiencing of self-relevant, past events. In this study, we used a novel VR system, which allowed us to create well-controlled, real life-like scenes into which 80 healthy participants were immersed during the initial stage of encoding and later retrieval. The main aim of the first experiment was to validate the VR paradigm to study episodic autobiographical memory in a naturalistic setting. In the second experiment, we tested whether the congruent multisensory bodily cues, i.e. the presence or absence of one's own physical body seen from first-person perspective, would impact episodic autobiographical memory performance. In a third control experiment, we tested whether the body-related changes in memory performance were related to multisensory bodily cues or could be replaced by any moving control object. The experiments had one main technological and one main scientific objective: a.) to create episodic autobiographical memory setting in the laboratory-based environment using immersive VR and b.) to examine whether multisensory bodily cues, which were previously shown to influence self-consciousness and egocentric, first-person view cognition, would modulate episodic autobiographical memory. Based on previous bodily self-consciousness work which has shown that body-related views enhance perceptual (Aspell et al., 2009; Noel et al., 2015) and egocentric cognitive processes (Canzoneri et al., 2016), here we have hypothesized that the presence of one's physical body would enhance memory performance. First, we showed that the immersive VR technology allows to test real life-like events in a well-controlled, laboratory-based setting. Second, we demonstrated that the presence of one's own physical body during encoding significantly enhances memory recognition and that this effect was body specific. These findings are further discussed in section 3.1.1.

1.4.2 Subjective self-experience in bodily consciousness and memory (study 2)

Remembering personally experienced events in vivid, multisensory detail involves integrating perceptual events and selecting meaningful spatiotemporal entities from the stream of experience into a specific conscious representation during memory retrieval (Bonnici et al., 2016). The subjective re-experiencing of past events is often described as re-living the past event from a viewpoint and location that is similar to that during encoding of the event (Nigro and Neisser, 1983; Rice and Rubin, 2011). Therefore, the two spatial components of bodily self-consciousness, the first-person perspective and self-location, are of particular relevance to episodic autobiographical memory (Bergouignan et al., 2014; St. Jacques et al., 2017). Studies of patients with lesions in the angular gyrus show that the lateral parietal cortex is critical for the subjective, conscious experience of retrieving multisensory episodic memories (Hower et al., 2014; Simons et al., 2010). Similarly, a number of reviews discuss the function of parietal lobe in bodily self-consciousness (Blanke, 2012; Blanke et al., 2015). Nonetheless, it is not known to what extent and whether bodily self-consciousness and autobiographical memories, either episodic or semantic, involve distinct or similar brain regions. In this study, we examined whether the activations in the inferior parietal lobule as observed in the study of Ionta et al. (2011), which experimentally manipulated the self-location and first-person perspective aspects of bodily self-consciousness, may anatomically overlap with the activations related to the subjective conscious experience of remembering self-relevant past events. We also included results from a lesion analysis (Ionta et al., 2011) of nine neurological patients suffering with out-of-body experiences with abnormal self-location and first-person perspective, whose brain damage was localized in the inferior parietal lobule. We performed a systematic quantitative meta-analysis of episodic and semantic autobiographical memories to investigate whether brain regions related to memory may share common neural substrates with bodily self-consciousness. We hypothesized that the first-person perspective and self-location of bodily self-consciousness are relevant to the autonoetic consciousness of episodic autobiographical memory and therefore we expected an anatomical overlap between these features in parietal regions. First, we showed an anatomical overlap bilaterally in the angular gyrus, specific to bodily self and episodic autobiographical self. Second, we showed no overlap between bodily self and semantic autobiographical self. These findings are further discussed in section 3.1.2.

1.4.3 The bodily self selectively and retroactively strengthens memory (study 3)

Many seemingly irrelevant everyday life events may become significant only later in time (Kensinger, 2015). For example, that stranger who asked for directions becomes more relevant after you realize that your wallet is missing. Studies on mental self-projections (Tulving, 1983; Arzy et al., 2008, 2009) suggest that the experience of the self in the present moment is also involved with the ability to remember our past or imagine the future. This conscious self-awareness (i.e. a mental state in which the content of one's consciousness refers to knowledge about oneself, for example reflecting about one's personality or identity) is intrinsically connected to the multisensory bodily processes (Blanke et al., 2015; Tacikowski et al., 2017). Recently, two behavioral studies showed how memory for neutral images can be enhanced by future fearful (Dunsmoor et al., 2015) or rewarding (Patil et al., 2017), conceptually-related events. More precisely, during the first stage of incidental encoding, the so-called "*pre-conditioning classification task*", two neutral categories of images portraying animals and tools appeared to be of the same relevance. During a second phase of the incidental encoding, the so-called "*conditioning classification task*", a prominent event, either fear conditioning or reward motivation, became purposefully associated with one of the two categories (animals or tools). A following memory recognition task revealed that participants remembered neutral images (for example tools) that were directly associated with fear or reward during the conditioning phase and they also remembered better the conceptually-related images (tools) from the pre-conditioning phase. In this study, which included 30 healthy participants, we examined whether the retroactive and selective effect could be a.) triggered by the multisensory bodily signals, such as the presence or absence of one's own physical body, b.) generalized to naturalistic scenes, such as inside rooms or outside scenes, into which the participants would be immersed using VR technology, rather than static, lab-based images. We expected that performance for contextual details in a one-hour delay memory recognition task would increase in the presence of bodily self-related cues (i.e. the presence of one's own physical body from the first-person viewpoint). First, we showed that the presence of one's own body can retroactively strengthen memory recognition. Second, we demonstrated that this retroactively enhancing effect became selectively associated with a particular group of items (either from rooms or scenes). These findings are further discussed in section 3.1.3.

1.4.4 Capturing thoughts with EEG and fMRI (study 4)

The temporal structure of spontaneous mentation is a key to the formation of a meaningful stream of consciousness. For example, when we daydream, an entire lifetime can continuously pass our minds in an hour. The human perception appears continuous, dynamic and unsegmented (Zacks et al., 2001). Recently, fMRI studies have proposed that functionally distinct sub-systems of the default mode network may be activated at the same time (Andrews-Hanna et al., 2010b; Axelrod et al., 2017). Yet, overwhelming evidence shows that information processing evolves through *a stream of discrete conscious units*, each representing *one specific mental state*. EEG microstate analysis investigates the temporal dynamics of large-scale neural networks (Michel and Koenig, 2018; Van De Ville et al., 2010). Furthermore, the duration and occurrence of EEG microstates regulate the quality of unconstrained mentation and provide an evidence for the electrophysiological segmentation of continuous brain activity into brief brain states (Baars, 2002a; Changeux and Michel, 2004; Michel and Koenig, 2018). In this study, we examined the spatiotemporal dynamics of large-scale brain networks associated to particular thoughts. 16 participants were instructed to direct their thoughts to their past, self-related memories or to mental, self-unrelated calculation, in order to examine the large-scale networks underlying the internal conscious thoughts. We examined *the spatiotemporal dynamics of brain activity* with high-resolution 7-Tesla fMRI and high-density EEG in two separate sessions. First, we studied the changes in BOLD activity for each brain region through the fractional amplitude of low frequency (fALFF) analysis and the interactions between those regions across time through functional connectivity analysis to examine if different functional regions become active at the same time. Second, we investigated the brief temporal organization of the large scale networks using the EEG microstate approach. Particularly, we examined the basic features of the EEG microstates: their duration, occurrence and the transitional probabilities. We expected that the fMRI data would confirm that the default mode network comprises distinct sub-systems. We then hypothesized that the EEG microstate analysis would reveal that these *functional networks are not continuous, but rather temporally parsed*. First, the fMRI data confirmed sub-networks of the default mode network are activated during episodic memory retrieval and these subnetworks show distinct connectivity patterns. Second, EEG microstate analysis showed specific microstates that increased in duration and occurrence during autobiographic episodic memory retrieval and during mental arithmetics. These findings are further discussed in section 3.1.4.

2 Studies

2.1 Study 1

First-person view of one's body in immersive virtual reality: influence on episodic memory

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ABSTRACT

Episodic autobiographical memories (EAMs) are recollections of contextually rich and personally relevant past events. EAM has been linked to the sense of self, allowing one to mentally travel back in subjective time and re-experience past events. However, the sense of self has recently been linked to online multisensory processing and bodily self-consciousness (BSC). It is currently unknown whether EAM depends on BSC mechanisms. Here, we used a new immersive virtual reality (VR) system that maintained the perceptual richness of life episodes and fully controlled the experimental stimuli during encoding and retrieval, including the participant's body. Our data reveal two classical episodic memory findings. Recognition memory for complex real-life like scenes decays with a delay and improves depending on the number of items that were changed between encoding and retrieval, validating the present VR system. We also report that delayed retrieval performance was enhanced when participants viewed their body as part of the virtual scene during encoding and that this body effect was not observed when no virtual body or a moving control object was shown, thereby linking the sense of self, and BSC in particular, to episodic memory. The present VR methodology and the present behavioral findings will enable the study key aspects of EAM, may benefit memory research in healthy participants, and also be of relevance for the understanding of memory disorders.

KEYWORDS: episodic memory, memory retrieval, real-life events, bodily-self

Introduction

A defining feature of episodic autobiographical memory (EAM) is the capacity to provide information about the content of our conscious personal experiences of “when” and “where” events occurred as well as “what” happened [1,2]. Previous studies defined EAM as the recall of contextually rich and personally relevant past events that are associated with specific sensory-perceptual and cognitive-emotional details [3–10]. EAM has been distinguished from semantic autobiographical memory, the latter being associated with general self-knowledge and the recall of personal facts that are independent of re-experiencing specific past events [11–17].

In a series of seminal papers, Endel Tulving highlighted the subjective dimension of EAM associated with the re-experiencing of specific past events by pointing out the importance of the sense of self and introducing his influential notion of autothetic consciousness. He argued that autothetic consciousness is of fundamental relevance to EAM, allowing one to mentally travel back in subjective time and recollect one’s previous experiences [2,18–20]. Tulving distinguished autothetic consciousness from noetic consciousness, linking the latter to semantic memory and semantic autobiographical memory and to knowing about (rather than re-experiencing) specific past events. Others extended Tulving’s notion of EAM and proposed that it is contributing to the sense of self across time [10,12,21–25] and developed behavioral tasks such as mental time travel [26–31].

Although, several other cognitive domains have been proposed to contribute to the sense of self (i.e. language, mental imagery, facial self-recognition [32–35], recent research has highlighted the importance of non-cognitive multisensory and sensorimotor contributions to the sense of self. This novel theoretical and experimental approach is based on behavioral [36,37], neuroimaging [38–40] and clinical data [39,41] and involves the processing and integration of different bodily stimuli to the sense of self: bodily self-consciousness (BSC); for review see [42,43]. BSC includes conscious experiences such as self-identification and self-location [36,37,44,45], as well as the first-person perspective [39,46,47]. This work was based on clinical observations in neurological patients with so-called out-of-body experiences characterized by changes in the sense of self, in particular of the experienced self-location and perspective from an embodied first-person perspective to a third-person perspective [39,41] and has been able to induce milder, but comparable, states in healthy subjects using virtual reality (VR) technology to provide multisensory stimulation [36,39,47].

Given the link of BSC with subjective experience and previous claims that subjective re-experiencing of specific past events is a fundamental component of EAM [2,18], we argue that multisensory bodily processing may not only be of relevance for BSC, but also for consciousness concerning past events. Recent findings have shown that BSC impacts several perceptual and cognitive functions such as tactile perception [48,49], pain perception [50,51], visual perception [52–54], as well as egocentric cognitive processes [55]. Concerning episodic memory, St. Jacques et al. [56] used a novel camera technology to examine the differences in self-projection (i.e. the capacity to re-experience the personal past and to mentally infer another person's perspective) and found that the ventral–dorsal subregions of the anterior midline are functionally dissociable and may differentially contribute to self-projection when comparing self versus other. Bergouignan et al. [57] reported that recall of EAM items and hippocampal activity during the encoding of episodic events is modulated by the visual perspective from where the event was viewed during encoding and St. Jacques et al. [58] showed that first- versus third-person perspective during retrieval modulated recall of autobiographical events and associated this with medial and lateral parietal activations. Together, these findings revealed that retrieval-induced forgetting is enhanced by third-person, but not first-person perspective. Therefore, these studies suggest that encoding of episodic memory requires the natural relationship between the body and the world, which is perceived from the first-person perspective. As such, we here predicted that bodily multisensory processing, that has been described to modulate BSC, would interfere with EAM processes.

Traditionally, behavioral and neuroimaging EAM studies rely on questionnaires, verbal reports, interviews, or mental imagery and predominantly investigated memory retrieval by using a variety of stimuli and procedures such as cue words and pictures [59–64]. For example, important research relied on interviews with the participants [61,65] on personalized lists of significant life events of participants [9,30,66–68], and employed different procedures asking participants to re-experience particular life episodes [59,62,63,69,70]. This differs from research investigating verbal memory through encoding and recall of word lists [71–74] or testing spatial memory with figures, spatial paths, or other visuospatial materials [75–77] (for which it is much easier to fully control encoding and retrieval). Beyond the use of controlled images, short video clips or words in EAM studies [4,78], an important line of neuroscientific EAM work has used novel approaches employing stimuli from real world encounters, outside the laboratory. For example, Cabeza et al. [79] created a campus tour paradigm and tested EAM retrieval by using digital photos taken from the tour. Similarly, Schacter et al. [80] introduced a museum tour paradigm, which was used to study the reactivation-induced updating in memory

for events experienced during the tour. Thus, during encoding, subjects went on an audio-guided museum tour, while wearing a camera which automatically took photos some of which were selected to test EAM (see also [56]). Vogel and Schwabe [81] also used pictures, which were taken automatically and continuously by a camera during a 2-hour walk through a zoo for testing EAM, comparing events represented by pictures from their own zoo tour with those of others. Several EAM research groups have relied on advances in video technology and VR during encoding and retrieval of information (i.e. spatial navigation[82,83]; social interactions[84,85]). Participants were seated in front of a computer screen showing a virtual environment and asked to navigate in such environments using a joystick (encoding) and later asked to recall selected objects from the environment (retrieval). These computer-based VR studies suggest that both interactions with the environment during encoding or retrieval influence memory performance. Compared to passive participation, several VR studies showed better learning performances across free recall trials and recognition tasks [82,86–88]. Plancher et al.[89] suggested that interactions with the naturalistic environment created with VR enhanced spatial memory. However, despite these important achievements, these virtual environments were mostly using non-immersive VR systems, did not employ real life like virtual scenes, and did not use VR technology that allows integrating the participants' body (and hence multisensory bodily stimulation) for the tested virtual life episodes. In the present experiments, we took advantage of a recently developed immersive VR system, which allows us to preserve the perceptual richness of life episodes, to fully control the experimental stimuli during encoding and retrieval, and to integrate and manipulate multisensory information of our participant's body in an online fashion. Our paradigm thus approaches 3D real life episodes as encountered during a person's life, but in a VR setting for which all items of the scene during encoding and retrieval are fully controlled. As such, this approach extends previous memory research, which studied the relation between episodic memory and autobiographical memory mainly by use of selected photographs. The present experiments had one major technological and one major scientific goal: (1) develop and test EAM-like memory in the laboratory with virtual episodes using immersive VR and (2) investigate whether multisensory bodily stimulations that have been shown to impact BSC, perception, and egocentric cognition modulates EAM.

In the first experiment, we tested our immersive VR system and sought to address some of the experimental limitations of earlier EAM studies, which either had limited control of actual autobiographical stimuli and events during encoding and only examined the stage of EAM retrieval [5,60,68,90] or controlled EAM encoding, but without the immersion into the original

scenes during EAM retrieval [9,57,66]. The main aim of our first experiment was to validate our novel VR paradigm in order to study EAM in a more naturalistic setting. We further tested EAM performance and confidence for immersive three-dimensional (3D) VR scenes at two different time points and for different number of objects (that changed between both sessions), we predicted memory decreases depending on delay and on the number of objects changed. Numerous behavioral cognitive studies have observed dissociations between memory accuracy and memory confidence [91–97]. For example, Talarico & Rubin [91] showed that the objective accuracy for events of September 11th, 2001 did not differ from accuracy in every-day events. However, the subjective feeling of remembering was enhanced for the highly arousing EAMs compared to everyday-like EAMs. Likewise, Sharot & Yonelinas [93] found that emotional photos were remembered with a greater subjective sense of recollection, yet the objective memory performance between emotional and neutral photos did not differ. Similar to the prior investigations examining the effect of emotional memories on subjective confidence, we thus sought to investigate the impact of multisensory bodily cues on subjective confidence.

In the second experiment, we investigated the main scientific hypothesis of the present experiments and tested the potential link between multisensory own body signals, that are fundamental for BSC and EAM. Vision and proprioception are sensory signals that are highly relevant for the brain in order to rapidly and continuously update the instantaneous representation of the body in space. Perceiving one's body as part of a visual scene (for example a hand lying on a table) relies on i. visual, ii. proprioceptive, and iii tactile cues. These signals are processed initially in different brain regions and subsequently integrated in multisensory brain regions (i.e. Blanke et al., 2015). Such multisensory body-related signals are not just relevant for hand perception, but also for BSC, including hand ownership (i.e. the feeling that this hand is mine), self-identification with the body, self-location (i.e. experiencing the self as being located in space), and the first-person perspective (i.e. experiencing the world from a spatial origin with a direction) [42,43,98]. We thus examined whether the presence of online and congruent multisensory cues from the subject's body (i.e. the presence of one's own physical body from the first-person viewpoint) impacts memory performance and confidence in the present VR paradigm, compared to an experimental condition where such online first-person bodily cues are absent. Based on BSC work that has shown that view of the body enhances perceptual and cognitive tasks [57,58] and based on the fact that during memory encoding the body is in most instances co-perceived with the other elements of the scene, we predicted that the presence of a body during encoding would enhance memory performance. Finally, we performed a third

(control) experiment in order to test whether the effect of multisensory bodily stimulation that we observed in the second experiment is specific to multisensory bodily cues.

Methods

Subjects

A total of 79 subjects with normal or corrected to normal vision were recruited to participate. None of the participants indicated neurological or psychiatric deficits and all subjects were right-handed. In experiment 1, 16 subjects ($M = 23.7$ years, $SEM = 0.7$ years, 8 female) participated in the immediate recognition group and 15 right-handed subjects ($M = 23.4$, $SEM = 0.8$, 7 female) participated in the one-hour delayed recognition group. In experiment 2, 16 subjects ($M = 26.8$ years, $SEM = 0.6$, 4 female) participated in the immediate recognition group and 16 subjects ($M = 24.5$ years, $SEM = 1.1$, 8 female) participated in the one-hour delayed recognition group. In experiment 3, 16 right-handed subjects ($M = 25.4$, $SD = 3.7$, 7 female) participated in one-hour delayed group. Sample size was derived from power analysis of previous BSC studies [99,100] and previous studies on mental time travel [28,30] indicating that 16 participants are sufficient for the present experiments. The study was approved by the local ethical committee and all three experiments were conducted in conformity with the Declaration of Helsinki. Informed consents were obtained from all our subjects.

Virtual Reality Technology

Our VR technology uses a spherical capturing and recording system and an immersive setup for first-person perspective (1PP) replay of the recorded real environments. For recording a scene, 14 cameras (GoPro Hero4) are assembled on a spherical rig (360hero 3DH3PRO14H) and linked to 4 pairs of binaural microphones (3DIO Omni Binaural Microphone) to cover the entire sphere of perception around a viewpoint (360° horizontally and vertically, stereoscopic vision, binaural panoramic audio). A custom software (Reality Substitution Machine, RealiSM, <http://lnco.epfl.ch/realism>) then aggregates all data into a single high-resolution panoramic audiovisual computer format (equivalent to more than 4 stereoscopic full HD movies). A head-mounted display (HMD, Oculus Rift DK2; 900×1080 per eye, $FOV \sim 105^\circ$ Vertical, 95° Horizontal) was used to immerse subjects into the recording and sound was administered with noise-cancelling headphones (BOSE QC15). Furthermore, the HMD was coupled with a stereoscopic depth camera (Duo3D MLX, 752×480 at 56Hz) mounted on its front face to capture subjects' bodies from 1PP. The RealiSM software then augments the fully immersive environment with a realistic view from which subjects could see their hands, trunk and legs from 1PP. As a result, subjects experienced as if they would be physically present in the pre-recorded

scenes and seeing oneself (not a 3D avatar). The software also allows integrating 3D virtual objects seamlessly in the scene (experiment 3).

Stimuli

Subjects were immersed in three (experiment 1) or two (experiments 2 and 3) pre-recorded rooms via the HMD (see below). For the encoding session, 10 everyday-life objects (e.g., coffee machine, pen, trash bin) were placed in each room. These real-life objects created the natural context of episodic memory at both encoding and retrieval. During retrieval, rooms remained either exactly the same as during encoding (i.e. the same 10 real-life objects were again presented at the same places in the previously visited rooms) or some of the objects (i.e. 1, 2 or 3 objects) were replaced by new objects that were not previously seen in any of the scenes. Each room included different set of objects in order to keep the same level of novelty and thus avoid any facilitation on the following recognition task.

Paradigm

Each of the three experiments consisted of two sessions, an incidental encoding period (session 1) followed by an immediate (group 1) or one-hour delayed (group 2) surprise recognition task (session 2). We studied incidental encoding (i.e. subjects were unexpectedly given a recognition test) in order to examine which of the every-day items would subjects remember without expecting the recognition test. In all three experiments, subjects were not informed that we would later test their memory for the stimuli encountered during the encoding session. Before the two experimental sessions, subjects were seated on a chair and asked to put on the HMD and headphones. Before the two experimental sessions, subjects were seated on a chair and asked to put on the HMD and headphones. In order to familiarize with the VR technology, each subject was immersed into an outside scene for 5 minutes, which we have recorded in a park close to the Lake of Geneva. We specifically asked our subjects to remain seated, turn and look around and to explore the scene as if they were sitting on a bench in the park. The lake scene consisted of a blue sky, there were trees behind them, and there was a view on the lake in front of them overlooking the French Alps on the other sides of the lake). Paradigm and testing sequence are depicted in **Figure 1A**.

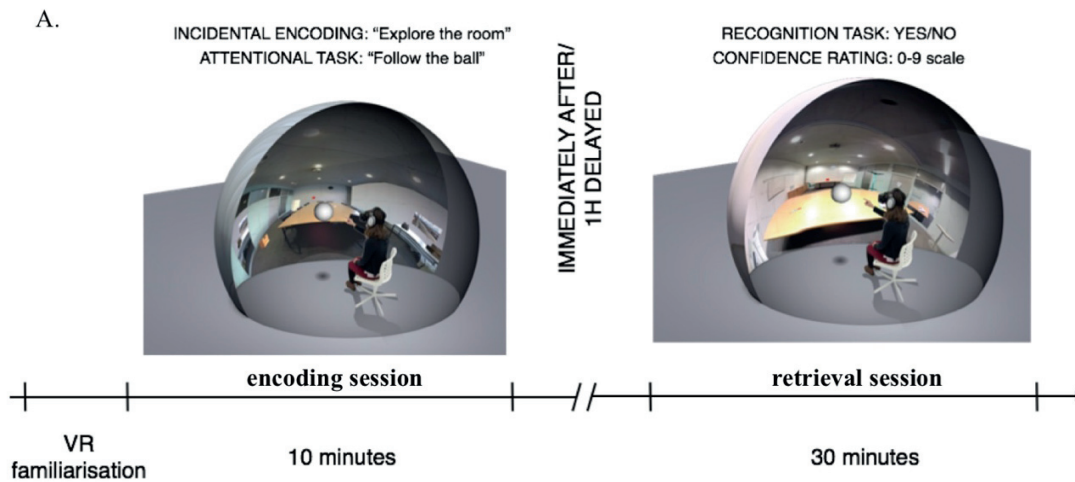


Figure 1A. Experimental procedure and 3D scenes. After a period of familiarisation with the immersive VR setup, participants performed the encoding session (10 minutes) during which they were exposed to different life-like 3D scenes. Scenes were characterized by a room that contained different objects (table, photocopy machine, pen, etc.). In experiment 1, one group of participants performed the retrieval session (30 minutes) immediately after the encoding session or after a one-hour delay (see main text for further detail).

Encoding Session

During the encoding session, to assure that subjects explored the entire room and to monitor their attention within the different 3D scenes (i.e. the different rooms), participants were instructed to freely explore each virtual room. Moreover, we programmed a virtual ball that appeared in each of the three rooms and was moving within the rooms for a duration of 30 seconds and covered all sections of the virtual room. Participants were asked to fixate the virtual ball and to follow its movements through the virtual room. In total, the target objects in the scenes, which were questioned during the retrieval session appeared at 6 different positions in each room. After the ball stopped moving, participants freely explored each room for another 30 seconds.

The procedure in experiment 2 was identical. However, in order to test the effect of viewing one's own body during encoding we asked subjects to follow the trajectory of the ball and to point at the moving ball with their hand and finger. The main manipulation consisted in showing the participant's physical body (body condition) or not (no-body condition). This was accomplished with the use of the stereoscopic depths cameras to capture in the participant's body and by turning them on in the body and off in the no-body condition. The participant's body was inserted in real-time in the virtual room and shown from the habitual visual first-person viewpoint. In the body condition, the subjects saw their physical hand, the trunk, and their legs (i.e. the stereoscopic depths cameras were turned on) in the HMD and as part of the virtual 3D scene (**Figure 1B**). In the no-body condition, the virtual 3D scene was identical except that the participant's body was

missing (i.e. the stereoscopic depths cameras were turned off) (**Figure 1C**). The order of presentation of the body and no-body condition was counterbalanced between subjects. In experiment 2 each participant explored two rooms (i.e. with 3 rooms as in experiment 1 the experiment would have been too long).

In experiment 3, participants were also asked to follow the movement of the ball appearing in each room (by physically pointing at it with their hand and finger). Yet in the object condition they were shown a non-bodily control object, instead of their own physical body (**Figure 1D**; see Supplemental video). The no-body condition was the same as in experiment 2. The presentation of the no-body and object condition was counterbalanced between subjects. No explicit instructions to memorize the objects of visited rooms were provided. In experiment 3, each participant explored two rooms (i.e. to keep conditions comparable with respect to experiment 2).



Figure 1B-D. The figure shows different conditions during the encoding session that we used in experiments 1-3 (the retrieval session was the same across all experiments). Thus, participants always saw the same 3D scenes on the head-mounted display, but the body of the participant was either not seen at all (Figure 1B; body condition), seen as part of the 3D scene (Figure 1C; no-body condition), or instead of the body a control object was seen (Figure 1D; control condition).

Retrieval Session

During the retrieval session, which was the same for all three experiments (i.e. no body or control object was shown), subjects were informed that they would be immersed in the same rooms again. They performed a total of three blocks of 40 trials (each lasting 10 seconds). Within the three blocks of 40 trials, we presented 10 trials, which were exactly the same as during the original encoding session (i.e. including the same 10 objects). The remaining 30 trials were different and had either 1, 2 or 3 new objects replacing the respective number of objects shown during the encoding session. The blocks and individual trials in each block were presented in a randomized order. Participants were free to re-explore the virtual scenes for 10 seconds, after which they were asked two questions that were shown on the HMD. First, participants performed a two-alternative forced choice task (yes/no) whether the virtual scene shown during the retrieval session corresponded to the virtual scene during encoding (recognition task) (“Is the scene exactly the same as when you first saw it?”). Participants indicated their response with a wireless computer

mouse. Second, participants were asked how confident they were about their answer (via a rating scale projected in the HDM; range from 0 (low) to 9 (high confidence)).

Statistical analysis

In experiment 1, an independent samples t-test for hit rate and false alarm rate was applied to test whether EAM performance differed depending on delay (i.e. immediate x one-hour delayed condition). Independent sample t-test were further used to analyze whether the hit rate and false alarm for EAM confidence ratings differed depending on delay. A mixed analyses of variance (ANOVA) with the number of objects changed (i.e. 1 object, 2 objects or 3 objects) and delay (i.e. immediate x one-hour delayed group) was performed. Further, a 2 x 3 mixed ANOVA was run to understand the effects of delay (i.e. immediate x one-hour delayed groups) and number of objects changed in a room (i.e. 1 object, 2 objects, 3 objects) for the EAM confidence for the false alarm rates. Where appropriate, Greenhouse-Geisser corrections of degrees of freedom were used. Significant ANOVA effects were explored by post-hoc tests using Bonferroni correction. The significance level was set to alpha 0.05.

In experiment 2, we performed a mixed analysis of variance (ANOVA) with delay (i.e. immediate x one-hour delayed groups) and body (i.e. body x no-body condition) on EAM performance for both hit rate as well as for false alarm rate. In order to investigate in more detail the effect of the number of objects changed across the different experimental conditions, we performed an additional analysis: 2 (i.e. immediate x one-hour delayed groups) x 2 (i.e. body x no-body condition) x 3 (i.e. 1 object, 2 objects or 3 objects) mixed analysis of variance (ANOVA), which was done only for the number of false alarms.

For EAM confidence, a 2 x 2 mixed ANOVA was performed with the factors retrieval time (i.e. immediate x one-hour delayed groups) and body (i.e. body present x body absent). Additionally, a three-way mixed ANOVA was run on the EAM confidence to gain more information about the effect of the number of objects changed specific to the false alarm rate. Where appropriate, Greenhouse-Geisser corrections of degrees of freedom were used. Significant ANOVA effects were explored by post-hoc tests using Bonferroni correction. The significance level was set to alpha 0.05.

In experiment 3, an independent samples t-test was applied to test whether EAM performance differed in the no-body versus object condition. This was done for hit rate and for false alarm rate.

An independent sample t-test was also used to examine whether EAM confidence false alarm differed in the no-body versus object condition. A mixed analyses of variance (ANOVA) with the number of objects changed (i.e. 1 object, 2 objects or 3 objects) and body (i.e. no-body x object) was performed. Similarly, a 2 x 3 mixed ANOVA was run to understand the effects of body (i.e. no-body x object) and number of objects changed in a room (i.e. 1 object, 2 objects, 3 objects) for the EAM confidence for the false alarm rates. Where appropriate, Greenhouse-Geisser corrections of degrees of freedom were used. Significant ANOVA effects were explored by post-hoc tests using Bonferroni correction. The significance level was set to alpha 0.05.

Results

Experiment 1 (Immediate versus one-hour delayed condition)

Participants in the delay group showed a significant decline in performance compared to the immediate memory recognition group. Mean hit rate was significantly lower in the delay group ($M = 55.5$, $SEM = 5.3$) than in the immediate group ($M = 73.1$, $SEM = 3.6$) ($t(29) = 2.7$, $p = 0.01$) (**Figure 2A**). False alarm rates did not differ between both groups (immediate group: $M = 31.4$, $SEM = 5.8$; delay group: $M = 23.3$, $SEM = 3.0$; $t(29) = 1.1$, $p = 0.2$) (**Figure 2B**). These data show that subjects recognized 3D scenic events better when tested immediately after the exposure than when tested with a delay of one hour, without any effect of delay on false recognitions.

Confidence ratings for hits in the immediate group ($M = 6.2$, $SEM = 1.6$) were not significantly different from those in the delay group ($M = 6.8$, $SEM = 1.3$) ($t(29) = 1.09$, $p = 0.2$) (**Figure 2C**). The same was found for false alarms confidence that did not differ between the immediate group ($M = 5.8$, $SEM = 0.4$) and delay group ($M = 6.4$, $SEM = 1.2$) ($t(29) = 0.7$, $p = 0.3$) (**Figure 2D**). Thus, despite changes in recognition, confidence did not differ depending on delay.

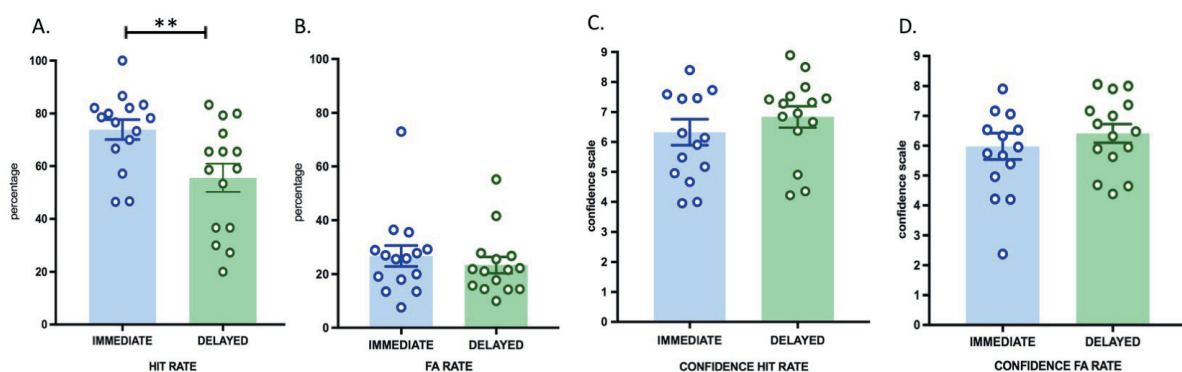
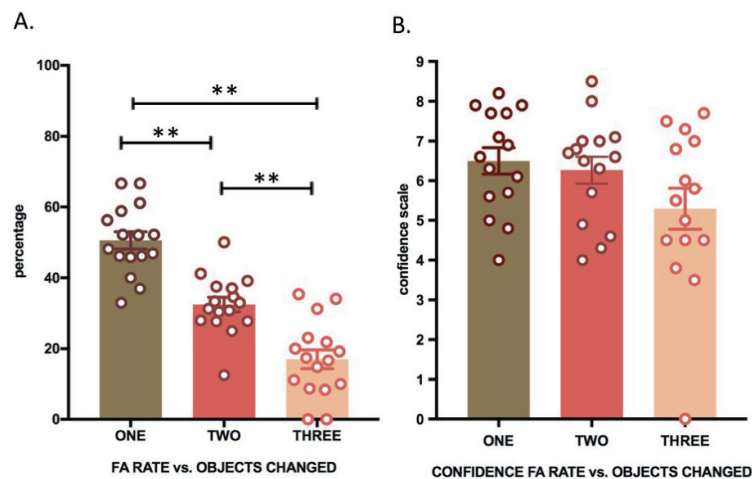


Figure 2. EAM performance in experiment 1 (immediate versus one-hour delay)

EAM performance (hit rate, false alarm rates) and subjective confidence ratings are indicated in percentage + SEM. (**) $P < 0.01$; (*) $P < 0.05$. Figure 2A. Hit Rate; Figure 2B. False Alarm Rate; Figure 2C. Confidence ratings (Hits); Figure 2D. Confidence ratings (False alarms). Blue color represents the immediate condition. Green color represents the delayed condition.

We next examined whether performance in the present task depended on the number of objects changed within each immersive 3D scene. This analysis was conducted on the false alarm rate (as no objects changed for hits, by definition). As predicted, analysis revealed a significant main effect for the number of objects changed ($F(2, 58) = 52.85$, $p < 0.0005$, partial $\eta^2 = 0.64$) (**Figure 3A**). Pairwise comparisons were performed for statistically significant main effects and revealed that subjects made progressively fewer false alarms with increasing number of objects (all p -values < 0.0005).

There was also a statistically significant main effect for the number of objects changed ($F(2, 58) = 4.163$, $p = 0.02$, partial $\eta^2 = 0.12$) (**Figure 3A**), revealing that subjects were progressively more confident in their performance with increasing number of objects that were changed between both sessions. These data show that subjects made more recognition errors and were less confident in conditions in which less objects were changed between encoding and retrieval.

**Figure 3. False alarms depend on number of items changed (experiment 1)**

EAM performance (false alarms) is indicated in percentage + SEM. (**) $P < 0.01$; (*) $P < 0.05$. Figure 3A. False Alarm versus Number of Items changed (i.e., 1 item, 2 items, 3 items); Figure 3B. Confidence Rate for False Alarm versus Number of Items changed (i.e., 1 item, 2 items, 3 items).

Experiment 2 (Body versus no-body condition)

Data for hit rates showed a significant two-way interaction between the time of retrieval and body conditions ($F(1,30) = 7.44$, $p = 0.01$, partial $\eta^2 = .19$). Post-hoc testing revealed that this effect was explained by a higher hit rate in the body, which was found specifically in the delay group (body: $M = 82.5$, $SEM = 8.2$; no-body condition: $M = 63.7$, $SEM = 8.2$; $t(15) = 2.51$, $p = 0.02$), but not in the immediate group (**Figures 4A and 4B**). The same analysis for false alarms rate did not reveal any differences $F(1, 30) = 0.002$, $p = 0.96$, partial $\eta^2 = .00$ (**Figures 4C and 4D**). These data show that recognition of immersive 3D scenes, that also include the first-person view of the subject's body, mimicking real-life experience is modulated and enhanced with respect to the same scenes without such a bodily view.

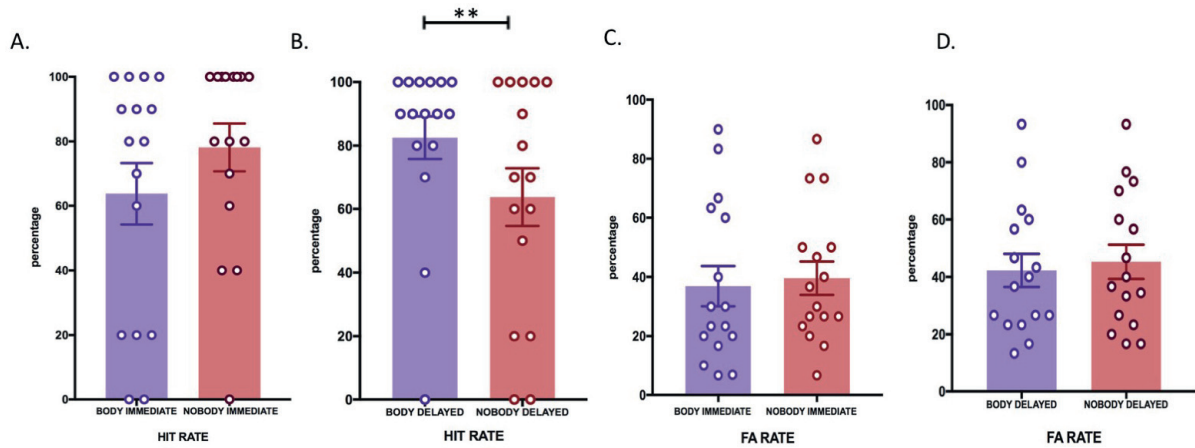


Figure 4. Body view enhances recognition (experiment 2)

Immediate versus one-hour delay EAM performance is indicated in percentage + SEM is indicated. (**) $P < 0.01$; (*) $P < 0.05$. Figure 4A. Hit Rate in immediate body (in purple color) versus immediate nobody (in pink color) condition; Figure 4B. Hit Rate in delayed body (in purple color) versus delayed nobody (in pink color) condition; Figure 4C. False Alarm Rate in immediate body (in purple color) versus immediate nobody (in pink color) condition; Figure 4D. False Alarm Rate in delayed body (in purple color) versus delayed nobody (in pink color) condition.

Confidence ratings for hits did not reveal any differences between the time of retrieval and body conditions ($F(1,30) = 1.06$, $p = 0.31$, partial $\eta^2 = .03$). The same analysis for false alarms also did not reveal any differences ($F(1,30) = 0.193$; $p = 0.66$, partial $\eta^2 = .00$). Thus, despite changes in recognition, confidence did not differ depending on time of retrieval or body conditions.

We also examined in more detail, whether memory performance (false alarms) in the immediate and delayed groups depended specifically on the number of objects changed and whether a body was seen or not. The analysis revealed a significant main effect for the number of objects changed

for the false alarm rate ($F(2, 60) = 27.48, p < 0.0005, \text{partial } \eta^2 = 0.47$). Pairwise comparisons were performed for statistically significant main effect and revealed that subjects made progressively fewer false alarms with increasing number of objects (all p 's < 0.0005). No statistically significant three-way interaction was found between the time of retrieval, body conditions and number of objects changed ($F(1.35, 40.54) = 1.84, p = 0.18, \text{partial } \eta^2 = 0.05$).

Similarly, we tested whether the confidence in the performance accuracy for both immediate and delayed groups (i.e. confidence ratings for false alarms trials) depended on the number of changed objects within each scene and the body condition. Results show that subjective ratings mirrored changes in memory performance. The main effect for objects showed a statistically significant difference for the number of objects changed ($F(2, 60) = 7.79, p = 0.01, \text{partial } \eta^2 = 0.2$). Post-hoc analysis revealed a statistically significant change from 1 object to 3 objects ($p < 0.0005$; Bonferroni corrected). There was no significant effect of body, nor significant three-way interaction was found ($F(1.85, 55.55) = 1.14, p = 0.32, \text{partial } \eta^2 = 0.03$). Thus, despite changes in recognition of 3D scenes depending on whether the subjects viewed their body during encoding or not, our subjects' confidence was equal across conditions. These data from experiment 2 show that subjects made more recognition errors and were less confident in conditions in which less objects were changed between encoding and retrieval, as in experiment 1.

Experiment 3 (object vs no-body condition)

There was no significant difference in hit rates for subjects in the object condition ($M = 70.0, \text{SEM} = 8.3$) compared to the no-body condition ($M = 70.0, \text{SEM} = 8.2$) ($t(15) = 0.00, p = 1.00$) (**Figure 5A**). Similarly, false alarm rates did not differ between groups (object group: $M = 46.2, \text{SEM} = 7.7$; no-body group: $M = 46.0, \text{SEM} = 6.5$; $t(15) = -0.05, p = 0.96$) (**Figure 5B**). These data show that recognition of immersive 3D scenes, where a non-bodily object, instead one's own body, is visible from the first-person view, does not modulate performance in the present task with respect to the same scenes without body or rectangular control object.

Confidence for hits in the object condition ($M = 4.8, \text{SEM} = 0.2$) was not significantly different from the no-body condition ($M = 4.4, \text{SEM} = 0.2$) (**Figure 5C**). Confidence for false alarm also did not differ between conditions (object condition: $M = 4.3, \text{SEM} = 0.3$; no-body condition: $M = 4.5, \text{SEM} = 0.2$) (**Figure 5D**).

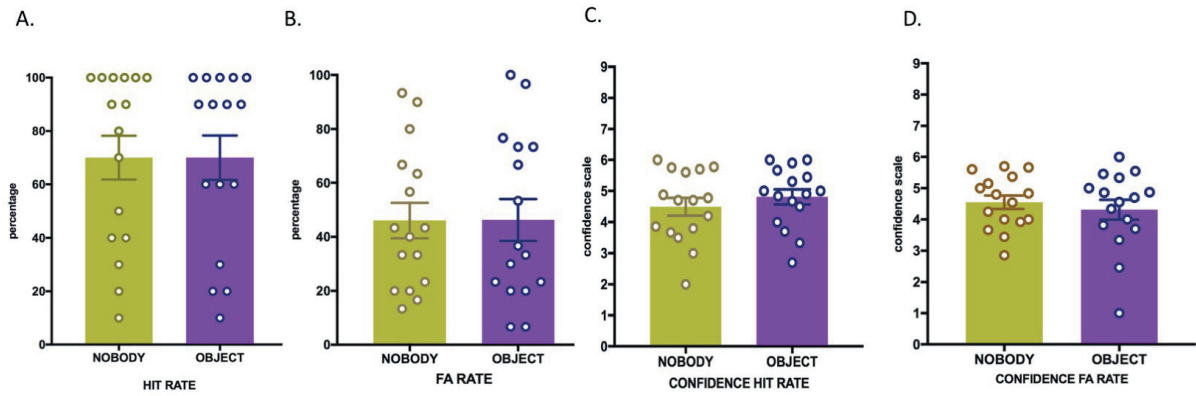


Figure 5. No difference between object and nobody view (experiment 3)

One-hour delay EAM performance is indicated in percentage + SEM is indicated. (**) $P < 0.01$; (*) $P < 0.05$. Figure 5A. Hit Rate for object versus nobody condition; Figure 5B. False Alarm Rate for object versus nobody condition; Figure 5C. Confidence ratings (Hits); Figure 5D. Confidence ratings (False alarms).

Further, we examined whether memory performance depended on number of objects changed and the body condition. The analysis revealed a significant main effect for the number of objects changed for the false alarm rate ($F(2, 30) = 7.79, p < 0.0005$, partial $\eta^2 = 0.34$). Post-hoc analysis revealed a statistically significant change from 1 object to 3 objects ($p = 0.01$; Bonferroni corrected). No statistically significant two-way interaction was found between the body conditions and number of objects changed ($F(2, 30) = 2.3, p = 0.11$, partial $\eta^2 = 0.13$). There was no significant difference between the no-body and object conditions.

We also tested whether the confidence in the performance accuracy depended on the number of changed objects within each scene and the body condition. The main effect for objects showed a statistically significant difference for the number of objects changed ($F(2, 30) = 3.42, p = 0.04$, partial $\eta^2 = 0.18$). Similarly, no statistically significant two-way interaction was found between the confidence ratings for the body conditions and number of objects changed ($F(2, 30) = 0.55, p = 0.58$, partial $\eta^2 = 0.03$).

Discussion

The present study allows us to draw three major conclusions. First, the present VR setup permits to measure recognition memory for 3D scenes that are immersive, rich in contextual detail, and that further integrates the moving body of the participant in online fashion. Our VR setup, thus, approaches real-life experiences in controlled laboratory conditions. Moreover, the present VR setup allowed us to project the same 3D virtual scenes during the encoding and retrieval sessions, providing us arguably with a level of experimental control that is comparable to examinations of classical word/picture-based recognition paradigms [101–104], which are typically used to study

memory. Second, applying this new setup we report that recognition memory for the tested VR scenes depends on the delay and on the number of changed elements between encoding and retrieval, comparable to findings for verbal and visual-spatial memory. Third, we show that viewing one's body as part of the virtual scene during encoding enhances delayed retrieval. This body effect was not observed when no virtual body was shown or when a moving control object (instead of the virtual body) was shown, suggesting that embodied views lead to body-related performance changes, as reported in studies investigating BSC.

An experimental VR setup that controls real-life like episodes during encoding and retrieval

Most prior laboratory-based EAM studies used cue words or images to trigger memory retrieval and mental time travel to the past in a controlled fashion [5,6,12,31,60,82,89,105–107]. However, these studies controlled only for memory retrieval but not for memory encoding [4]. Contrary to these previous studies, we exposed our participants to rich and immersive real-life scenes without the need for explicit mental time travel. Unlike earlier computer-based scenarios, we also did not present participants with artificial scenarios (simulated events in 3D), but immersed them into 360° video recordings of everyday real-life scenes that we digitalized for the encoding and retrieval sessions. Using the present naturalistic and controlled VR setup, we ensured that our participants experienced virtual 3D scenes with congruent multisensory bodily information (visual, motor, vestibular); these approach real-life experience as compared to classical virtual computer game tasks that have been used for episodic memory investigations in the past [108,109]. Thus, the present VR technology and future improvements of it will open new possibilities for conducting episodic memory research under ecologically valid experimentation in the laboratory by providing not only the ability to precisely design all stimulus aspects, but also to replay fully controlled sequences of real-life events.

Delay and number of changed objects modulates recognition memory performance

Our data reveal two classical episodic memory findings. Recognition memory for real-life like scenes decays with delay and improves depending on the number of items that were changed between encoding and retrieval. Previous EAM research is compatible with these findings, but has not been able to test or quantify this directly. By definition, the autobiographical memories of each individual differ and cannot be reproduced across participants and studies. As such, our VR approach allows for more control of the environment, in particular the use of the exact same context for both the encoding and the retrieval phase as well as a digital method to manipulate and control the 3D stimulus material. Combining immersive VR with memory research thus allowed us to get both high control and reproducibility, while allowing to test real-life like

scenes and events as compared to standard retrieval tasks. Specifically, while associative recognition memory for words or pictures [110–112] and EAM [96,97,113] has been tested for different memory delays, previous VR-based paradigms, investigating the formation of episodic memory of lifelike events, mostly tested immediate memory performance [83,84,114,115] (but see [116]). The present findings can be compared with classical memory findings for verbal and pictorial material where increasing delays increases forgetting [18,92,93,117,118] and with spatial memory work, where active navigation reduces forgetting as compared to passive viewing [82,86,87,89]. Thus, although we only tested short delays (i.e. one hour), our data show that subjects remembered 3D scenes better when tested immediately after encoding as compared to delayed retrieval. Our second predicted finding that recognition memory was better when more items were changed between the encoding and retrieval is also compatible with classical findings concerning the recognition of visual changes when testing long-term memory for spatial scenes, complex figures (including faces), or short texts [119,120], further revealing the experimental validity of the present setup for research in episodic memory.

Embodiment and episodic memory of life-like events

Besides reproducing classic memory effects, the present study also reveals a new finding, i.e. that memory is better when the body is visible at the encoding. Research on embodiment and BSC has used several VR paradigms and revealed the influence of multisensory and sensorimotor bodily input and has highlighted the importance of the view of the observer's body [43]. Such research showed that BSC can be modulated by showing the body or body parts of the participant from different first-person viewpoints compared to showing no body at all. Moreover, this effect has been shown to be body-specific by demonstrating that different non-corporeal objects shown from the same position and viewpoint do not alter BSC [43]. Here, we extend this BSC principle to memory research by showing in experiment 2 that the recognition of 3D scenes that included within the first-person view also the subject's body (as is characteristic of normal everyday perception) was modulated and significantly enhanced with respect to the same scenes without such a bodily view. This is compatible with previously reported effects for multisensory bodily perception [48,49] and BSC [37,39,44]. These BSC studies showed that visuo-tactile perception, as well as self-identification and self-location towards a seen human body or body part are enhanced when the body is shown in congruent position with respect to the subject's body. Accordingly, we argue that the present body effect on the recognition memory of 3D scenes is comparable to similar effects in multisensory perception and BSC (i.e. for review see [43]) as well as a number of cognitive processes, where self-related bodily information is critical. For

instance, viewing the body increases tactile perception [121], modulates interpersonal tactile responses [122,123], affects social cognition [124,125], and concept processing [55].

The post-encoding modulation of EAM performance at a delay due to the presence of bodily-self

It is of relevance to point out that the enhancement of EAM performance in the body present condition was observed only in the one hour delayed retrieval session, but not when the retrieval followed immediately after the encoding session. Most events that people experience during their daily life will be forgotten. What determines which of the every-day experiences will be remembered? It has been well demonstrated that people tend to remember better those life-episodes, which are distinct and personally meaningful and, of importance for the present study, relate to the self or self-consciousness [21,28,30,126–129]. Additionally, the ability to discriminate among similar experiences is a crucial feature of episodic memory [130]. As such, the encoding while viewing one's body may provide a better separation of memory traces than an encoding without a body as the multisensory integration of congruent signals from the body generates a more distinct target pattern to compare to the lures. Moreover, the typical delay for hippocampal consolidation processes continues beyond approximately one hour (for shorter delays it may rather relate to short-term memory, relying distinct mechanisms) [131–134]. Accordingly, we argue that enhanced self-relevance and recruitment of BSC-related processing in the present experiment (by viewing one's body during encoding) improves the consolidation process of episodic memories, but not shorter-spanned memories. Similar delay-only effects have also reported during other manipulations. Thus, Sharot & Yonelinas [93] showed that emotion had no effect on recall when tested immediately after encoding, but only after a delay. Future work, including neuroimaging should investigate whether the modulation of delayed recall as described in the present experiments and those by previous authors rely on similar or distinct mechanisms. This testing may also include the investigation of additional BSC constraints (i.e. peripersonal space and embodiment [43,49,135]).

It could be argued that the enhanced EAM performance of experiment 2 could relate to differences in the amount of visual information provided in both conditions (higher in the body versus the no-body condition) or higher salience or attention due to the additional inclusion of the tracked body in the body condition. First, we note that addition of the tracked body actually covers or hides parts of the virtual scene and may have thus incidentally hid some of the changed items and should thus rather decrease recognition memory. Yet, the opposite was observed in experiment 2. However, in order to formally investigate the potential role of differences due to vision or

attention between conditions we compared, in experiment 3, the no-body condition with a condition in which subjects viewed a non-bodily control object that was moving congruently with the participant's body in real-time. Data from this experiment revealed no memory improvement in the object condition, arguing against a visual or attentional account and further corroborating our proposal that the present recognition enhancement is due to multisensory-motor bodily stimulation that has been shown to be crucial for BSC [36,42,49,136] and characteristic of normal everyday experience. These data also argue against the possibility that the present body effect on recognition memory can be generalized to an embodied object as the object condition did not induce any performance changes. Future EAM studies should investigate other BSC aspects, such as peripersonal space, embodiment, and visual-proprioceptive alignment [43]. By revealing bodily effects in the present EAM paradigm, we thus link BSC to EAM, extending earlier memory work [57] that has focused on contributions of the first-person perspective in autobiographical memory or of vestibular processing on EAM [137]. Finally, based on these data we argue that the brain mechanisms of BSC are linked to those of autothetic consciousness that are of fundamental relevance to EAM. Autothetic consciousness is the ability to mentally travel back in subjective time and recollect one's previous experiences [2,18–20] and the present data suggest that multisensory bodily processing during encoding and remembering are not only of relevance for the conscious bodily experiences of self-identification, self-location, and first-person perspective [36,37,39,44–47], but also autothetic consciousness.

Confidence and episodic memory

Does confidence mimic these changes in episodic memory performance? We report, as predicted, that confidence increased jointly with memory recognition improvements for conditions in which more objects were changed. This finding is in line with several studies showing that confidence in everyday, non-arousing EAM, measured by remember/know paradigms and recollection questionnaires, declines together with the objective memory performance [97,110,113]. However, our data also show that confidence levels dissociate from memory performance, as delay dependency and the view of one's body (experiment 2) during encoding modulated recognition memory, but not confidence levels. Further research needs to target objective memory performance and subjective confidence using real-life scenes as tested with the present VR setup. The differential delay- and body-effects in the present study suggest that memory performance and confidence rely on distinct functional mechanisms [138], potentially consistent with the classical two-component model of episodic memory highlighting the distinction between familiarity and recollection, with only the second leading to changes in confidence [112].

Outlook

The present VR methodology and the present behavioral findings will enable to study several key aspects of EAM, including its subjective, behavioral and neural mechanisms and may benefit basic memory research in healthy participants, the understanding of memory disorders, and potentially provide therapeutic options. Concerning the involved brain mechanisms of BSC-EAM interactions it will be important to describe how BSC related neural systems described for body ownership and self-identification [139,140], self-location and first-person perspective [39,141], as well as for temporal aspects of self-related processing [24,140] will interact with the well-described memory circuits in the medial temporal lobe. However, as the typical encoding of everyday life events is always associated with multisensory information involving the body (only few of which we tested here), more detailed investigations are necessary, involving BSC constraints [43]. Moreover, beyond bodily cues, the present setup also allows to control, auditory, visual cues, social cues and language material during encoding and retrieval and thus to test its effects on EAM in in rich real-life like scenarios. The same techniques could also be extended and adapted to the investigation of amnesic patients. Future work may study in particular the links between autothetic consciousness and BSC. Finally, there is a growing interest in VR for education (e.g. neurosurgery, firemen, pilots), cognitive behavioral therapy (e.g. treating phobias or post-traumatic stress disorder), and as pain treatments [142,143]. Future work is needed in order to explore the differences between VR and traditional studies in terms of learning and performance. Adaptations of the present setup will allow to personalize memory scenarios for a given memory patient and may be beneficial in memory rehabilitation [144,145].

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2.2 Study 2

Common recruitment of angular gyrus in episodic autobiographical memory and bodily self-consciousness

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ABSTRACT

Parietal cortex and adjacent parts of the temporal cortex have recently been associated with bodily self-consciousness (BSC). Similarly, growing evidence suggests that the lateral parietal cortex is crucial for the subjective aspects of episodic autobiographical memory (EAM), which is based on the conscious experience of reliving past events. However, the neuroanatomical relationship between both fundamental aspects remains currently unexplored. Moreover, despite the wealth of neuroimaging data on EAM, only few neuroimaging studies have examined BSC and even fewer examined those aspects of BSC that are most closely related to EAM. Here we investigated whether regions in the inferior parietal lobule (IPL) that have been involved in spatial aspects of BSC (self-location and first-person perspective), as described by Ionta et al., are also active in studies investigating autobiographical memory. To examine this relation, we thus compared the regions indicated in the study by Ionta et al., based on data in healthy participants and neurological patients, with the results from a meta-analytical study we performed based on functional neuroimaging studies on EAM and semantic autobiographical memory (SAM). We report an anatomical overlap bilaterally in the angular gyrus (AG), but not in other parietal or temporal lobe structures between BSC and EAM. Moreover, there was no overlap between BSC and SAM. These preliminary data suggest that the bilateral AG may be a key structure for the conscious re-experiencing of past life episodes (EAM) and the conscious on-line experience of being located and experiencing the world in first-person (BSC).

Keywords: multisensory integration, parietal cortex, bodily self-consciousness, out of body experience, episodic autobiographical memory, ALE meta-analysis, fMRI, lesion analysis

1. Introduction

The subjective feeling of a unified self that is experienced as residing in one's own body, which is localized at a specific position (self-location) and from where one perceives the world (first-person perspective) defines the three major components of multisensory bodily self-consciousness (BSC) (Blanke et al., 2015; Blanke and Metzinger, 2009). Although the experimental investigation of BSC and the underlying brain networks remains a challenge, recent advances in digital technologies have provided compelling ways of successfully inducing illusory states of BSC in healthy individuals by manipulating multisensory bodily cues (Ehrsson, 2007; Lenggenhager et al., 2007b; Petkova and Ehrsson, 2008). Recently, illusory self-location and first-person perspective were manipulated in a fMRI study (Ionta et al., 2011) by applying tactile stroking to the back of a participant, while simultaneously displaying the stroking on the back of a virtual body via a head mounted display. Such experimentally-induced changes in BSC have been linked to activity at the temporo-parietal junction (TPJ; Brodmann area 39/40). Likewise, lesions, seizures or electrical brain stimulation in the TPJ area also result in changes in self-location and first-person perspective (Blanke et al., 2002, 2004; De Ridder et al., 2007; Ionta et al., 2011). Thus, patients suffering from so-called out of body experiences (OBE) caused by brain damage at the TPJ, subjectively experience the world from an illusory disembodied self-location with an inverted direction of first-person perspective and they self-identify with this elevated position (Blanke and Arzy, 2005; Heydrich and Blanke, 2013; Ionta et al., 2011).

The subjective sense of self in time that enables us to re-experience ourselves in the past and mentally project ourselves into the future, i.e. autonoetic consciousness, has been considered the defining aspect of episodic autobiographical memory (EAM) recollection (Tulving, 1985). Traditionally, since the discovery of severely amnesic patients with damage to the medial temporal lobe (MTL) (Scoville, 1957; Steinvorth et al., 2005), many fMRI studies confirmed the essential role of MTL structures in memory (Cabeza et al., 2007; Clark and Maguire, 2016; Daselaar et al., 2008; St. Jacques et al., 2015; Svoboda et al., 2006). Relevant to the present study, numerous neuroimaging studies on episodic memory (Bellana et al., 2017; Cabeza and St Jacques, 2007; Gilmore et al., 2015; Rugg and Vilberg, 2013; Rutishauser et al., 2017; Sestieri et al., 2011, 2017; St Jacques et al., 2013) also reported persistent and robust activations in the lateral parietal cortex, particularly the angular gyrus (AG; Brodmann area 39). Interestingly, patients with lateral parietal lesions are successful in objective EAM tasks, however, it has been found that the vividness, richness and subjective confidence in experiencing their personal memories is diminished (Berryhill et al., 2007; Hower et al., 2014; Rugg and King, 2017; Simons et al., 2010). These neuropsychological, fMRI and TMS studies suggest that the sole engagement of MTL structures may not be sufficient for the multi-modal

and conscious experiences, which accompany subjective, detail-rich and self-related EAM recollection, and that additional regions, such as those in the lateral parietal cortex, are involved as well.

The activity in the angular gyrus has also been associated with semantic memory (Binder et al., 2009; Bonnici et al., 2016; Humphreys and Ralph, 2017; Seghier et al., 2010). Recent resting state function connectivity MRI studies proposed that the lateral parietal cortex, particularly the AG, may represent a heterogeneous area comprised of functionally and anatomically distinct sub-regions (Daselaar et al., 2013; Nelson et al., 2010, 2013; Seghier, 2013), also questioning whether AG supports the same processes during episodic and semantic retrieval. Critically, Brown et al. (2018) demonstrated that the left posterior parietal cortex contributes to both EAM and SAM, but each demonstrating divergent activities. More specifically, the AG exhibited a graded pattern of activity, declining from episodic recollection to correct rejections of novel events in semantic remembering. Consistent with the prior literature, we therefore hypothesized that SAM (i.e. the general self-awareness of personal facts), which is independent of re-experiencing particular, conscious, vivid and multi-modal life episodes, would not anatomically overlap with BSC activations in lateral parietal cortex.

Given the link of BSC with subjective experience and seminal proposals by Endel Tulving that subjective re-experiencing of specific past events is a fundamental component of EAM (Tulving, 1985, 2005), BSC and autonoetic consciousness may share neural mechanisms. As subjective re-experiencing of own life events is often characterized by a viewpoint and location from where the event is re-experienced, it may be argued that the two spatial components of BSC (first-person perspective and self-location) are of particular relevance for EAM. Moreover, St. Jacques et al. (2017) showed (using different methodology) that first-versus third-person perspective during memory retrieval modulated recall of autobiographical events, associated with lateral parietal activations, potentially overlapping with BSC activations. Despite several reviews discussing the role of parietal lobe in BSC (Blanke, 2012; Blanke et al., 2015; Serino et al., 2013) as well as the recent interest in the contribution of parietal lobe to EAM (Igelström and Graziano, 2017; Moscovitch et al., 2016), it is currently unknown whether and to what extent BSC and autobiographical memories (episodic or semantic) engage the same or distinct brain regions. In order to provide preliminary data, we investigated the question of overlap between the spatial aspects of BSC and EAM by studying whether the activations in IPL and the adjacent parts of the posterior temporal cortex during the experimental manipulation of both aspects of BSC, as observed in the study by Ionta et al., (2011) in healthy subjects, overlap with

those described in EAM studies. We further included results from a lesion analysis study of nine neurological patients with OBEs (abnormal self-location and abnormal first-person perspective) whose brain damage was also localized at TPJ. We performed a systematic quantitative coordinate based meta-analysis (Eickhoff et al., 2009, 2012) on human EAM as well as SAM functional neuroimaging studies to examine whether and where brain regions associated with autobiographical memories share common or distinct neural substrates with BSC as reported in the study by (Ionta et al., 2011). Based on the evidence that both EAM and BSC recruit the lateral parietal cortex and given the fundamental link between BSC and EAM with multi-modal subjective and conscious experiences, we hypothesized that there would be an anatomical overlap in this structure between BSC and autobiographical memory, specifically for the episodic (EAM), but not the semantic aspects (SAM). Consistent with the prior literature, EAM would be related to BSC in the posterior parietal cortex, particularly the AG region, because of its role in integrating cross-modal, multi-sensory features to form a unified episodic memory representation, which is fundamentally related to multi-sensory BSC signals (i.e. particularly the first-person perspective and self-location).

2. Methods

2.1 Experimental and clinical studies on bodily self-consciousness (BSC)

We evaluated data from our previously performed fMRI study in twenty-two healthy subjects ($M = 25.4$, $SD = 5.7$, 22 male), assessing neural mechanisms of BSC using multisensory stimulation. In this study, Ionta et al. (2011) experimentally manipulated two global aspects of BSC (self-location and first-person perspective) by using an MRI-compatible robot. Based on the original study by (Lenggenhager et al., 2007a), which used virtual reality technology (VR) to experimentally manipulate BSC, (Ionta et al., 2011) applied synchronous tactile stimulation to the participants' back while lying in the MRI scanner. Participants observed a full body avatar being stroked congruently on its back from a third-person perspective. After synchronous visuo-tactile stimulation, participants showed higher self-identification towards the virtual body, as compared to the asynchronous condition. Furthermore, about half of the participants experienced an upward looking first-person perspective (compatible with the physical orientation of their body), while the remaining half of the participants had the impression to be looking down (down-ward-looking perspective). This perspective was incompatible with the orientation of their body, compatible with a third-person perspective induced by the full-body illusion. Moreover, the study by (Ionta et al., 2011) also included results from lesion analysis

of nine neurological patients, suffering from a carefully defined altered state of BSC, namely out-of-body experiences (OBEs) caused by focal brain damage (OBEs are characterized by abnormal self-location and abnormal first-person perspective). By normalizing each patient's lesion into common reference space, statistical lesion overlap comparison was carried out, contrasting the lesions of the OBE-patients with those from a control group using voxel-based lesion symptom mapping (VLSM; Bates et al., 2003). For more details, see Supplementary information in Ionta et al. (2011).

2.2 *Selection of studies and inclusion criteria for EAM and SAM meta-analyses*

For both the episodic as well as the semantic autobiographical memory studies, we conducted a comprehensive and systematic search of the literature using PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) and Web of Knowledge (<http://wokinfo.com>). The following combination of keywords was used for episodic autobiographical memory: “autobiographical memory”, “episodic”. For the semantic autobiographical memory, we selected: “autobiographical memory”, “semantic”. The reference lists of the included studies and several previous meta-analyses were used to find studies (Kim, 2016; Martinelli et al., 2013; Svoboda et al., 2006). Studies using positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) were included in the analyses. Studies were considered only if activation coordinates were reported in standardized Montreal Neurological Institute (MNI) or Talairach (TAL) coordinates and the analysis reported on the whole brain. All Talairach coordinates were transformed into the MNI coordinates using a linear transformation (Lancaster et al., 2007).

Only study results in healthy subjects with no neurological or psychiatric disorders, brain lesions or pharmacological manipulations were considered. Studies including both younger and older healthy participants were included in the analysis. No single subject studies were considered for the analyses. If articles reported several experiments with independent samples, then these experiments were considered individually in the analysis. Visual as well as auditory cues were included irrespectively of their emotional valence. Both recent and remote memories for the EAM analysis were included. Personal events and judgments of the self-versus others were included in the SAM analysis.

2.2.1 *Episodic (EAM) and semantic (SAM) autobiographical memory studies*

Forty-one experiments investigated EAM (**Supplementary Table 1**) and this meta-analysis included 588 foci and 813 subjects. We focused primarily on studies investigating self-related, personally-

relevant EAM irrespective of their specificity, age or control task. Thus, we included both recent and remote EAM (e.g., Addis et al., 2012; Oddo et al., 2010), using semantic memory (Donix et al., 2010; Holland et al., 2011) as well as low level baseline condition (e.g., rest or pseudo words) (Nadel and Moscovitch, 1997; Piolino et al., 2008) as control tasks. We selected twenty-five experiments examining SAM (**Supplementary Table 2**) and included 314 foci and 396 subjects. Particularly, we included studies investigating familiar, self-relevant semantic information (e.g., faces, places, objects), but also self-trait judgements (Sugiura et al., 2009, 2011). Control task in the SAM category included unfamiliar information or other-trait judgements (e.g., Gutchess et al., 2007; Jenkins et al., 2008).

2.3 Data analysis for EAM and SAM studies

We employed the quantitative activation likelihood estimation (ALE) algorithm as implemented in the GingerALE software, v2.3.6 (Eickhoff et al., 2009, 2012; Turkeltaub et al., 2012). The ALE algorithm ultimately aims at assessing statistically whether a specific task activates each specific voxel of the brain more likely than by chance (Eickhoff et al., 2009). To account for spatial uncertainty in the location of activity, each voxel at the location of the peak-activation from each contrast and experiment is convolved with a 3-dimensional Gaussian kernel whose full-width at half maximum is weighted by the number of subjects used in that particular experiment. The sum of these Gaussians constitute the modeled activation (MA) maps. We used a within-cluster $p < 0.05$ FWE correction with $p < 0.001$ uncorrected as the cluster-forming threshold. The minimal cluster size was set to 200mm^3 . Visualization of foci and the activation clusters from the above mentioned analyses was performed using MRICron software (<http://people.cas.sc.edu/rorden/mricron/index.html>) and the clusters were labeled using the Automated Anatomical Labeling (AAL) atlas (Tzourio-Mazoyer et al., 2002) and Brodmann atlas implemented within the same software.

3. Results

3.1 EAM regions (individual ALE analysis)

The ALE meta-analysis of the forty-one EAM studies uncovered ten clusters (**Table 1**). More specifically, we found activation bilaterally in the angular gyrus (AG, Brodmann area 39) and the left superior temporal gyrus (STG, Brodmann area 22). We found consistent activations in cortical midline structures, i.e. bilaterally in the ventral and dorsal parts of the posterior cingulate cortex (PCC; Brodmann areas 31 and 23) and left anterior cingulate cortex (ACC, Brodmann area 10). The analysis also revealed activity bilaterally in the hippocampi and adjacent parahippocampal gyri (PHG; Brodmann

areas 28, 35, 36) and in the left inferior temporal gyrus (ITG, Brodmann area 21). Other clusters were found in the left inferior frontal gyrus (IFG, Brodmann area 47), bilaterally in superior frontal gyrus (SFG, Brodmann area 32) and in the left middle frontal gyrus (MFG, Brodmann area 6).

Brain region	Hemisphere	Size (mm3)	x	y	z	Brodmann area
Superior Temporal gyrus	L	192*	-54	-32	20	39, 40
Superior Temporal gyrus	R	197*	55	-28	16	39, 40
Temporal Parietal Junction	R		54	-52	26	39, 40

Table 1. Results from BSC experimental study (N=22) FDR-corrected, $p < 0.05$ and neurological patients study (N=9) based on voxel-based lesion symptom mapping (VLSM) FDR-corrected, $p < 0.01$.

R= right, L= left, B= bilateral; x, y, z are the coordinates in MNI space. Label provided using the Brodmann atlas. *Active cluster size in voxels.

3.2 SAM regions (individual ALE analysis)

The ALE meta-analysis of the twenty-five SAM studies uncovered two clusters (**Table 2**). These were located in the cortical midline structures, i.e. bilateral ventral and dorsal parts of the ACC (Brodmann areas 32, 24) and bilaterally in the ventral and dorsal PCC (Brodmann area 31 and 23). There was no activity in the region of the angular gyri.

Brain region	Hemisphere	Size (mm3)	x	y	z	Brodmann area
Angular gyrus (TPJ)	L	3696	-48	-62	22	39
Angular gyrus (TPJ)	R	1040	60	-60	20	39, 22
Posterior cingulate cortex	B	10248	-4	-58	26	31, 23
Anterior cingulate cortex	L	2536	-4	58	-12	10
Parahippocampal gyrus	L	10528	-24	-16	-20	28, 36
Parahippocampal gyrus	R	6200	20	-20	-16	35, 36
Inferior temporal gyrus	L	2176	-62	-8	-20	21
Inferior frontal gyrus	L	3072	-36	24	-12	47
Superior frontal gyrus	B	2248	8	20	52	32
Middle frontal gyrus	L	1176	-40	8	42	6

Table 2. Results from EAM meta-analysis. Within-cluster FEW-corrected $p < 0.05$ with $p < 0.001$ (uncorrected) as the cluster forming threshold. R= right, L= left, B= bilateral; x, y, z are the coordinates in MNI space. Label provided using the Brodmann atlas.

3.3 Anatomical overlap between BSC, EAM and SAM

The BSC regions from the fMRI study on healthy subjects by Ionta et al. (2011) were located at the left and right temporo-parietal junction (TPJ) and included the posterior part of the

superior temporal gyrus, the parietal operculum, the posterior insula and superior portion of the supramarginal gyrus (lTPJ MNI: -54, -32, 20; rTPJ MNI: 55, -28, 16). The quantitative lesion analysis of the patient data in Ionta et al. (2011) revealed a maximal lesion overlap at the rTPJ and included the posterior end of the superior and middle temporal and angular gyri (MNI: 54, -52, 26), which was located somewhat posterior to the fMRI-based BSC regions. The union of the regions from the fMRI and lesion analyses defined our BSC regions (**Table 3**).

Brain region	Hemisphere	Size (mm ³)	x	y	z	Brodmann area
Anterior cingulate cortex	B	5032	-6	44	4	32, 24
Posterior cingulate cortex	B	1504	2	-60	20	31, 23

Table 3. Results from SAM meta-analysis. Within-cluster FWE-corrected $p < 0.05$ with $p < 0.001$ (uncorrected) as the cluster forming threshold. R= right, L= left, B= bilateral; x, y, z are the coordinates in MNI space. Label provided using the Brodmann atlas.

We found an anatomical overlap between EAM regions and BSC regions bilaterally in the angular gyrus (Brodmann area 39) (**Figure 1A**). The size of the anatomical overlap between BSC and EAM was 1192mm³ on the left side and 128mm³ on the right side. EAM and SAM overlapped in the ventral and dorsal parts of the PCC (Brodmann areas 31 and 23) and bilaterally in the dorsal part of ACC (Brodmann area 32) (**Figure 1B**). The size of the anatomical overlap between the ventral and dorsal parts of the PCC was 776 mm³ and 560 mm³ in the dorsal part of the ACC.

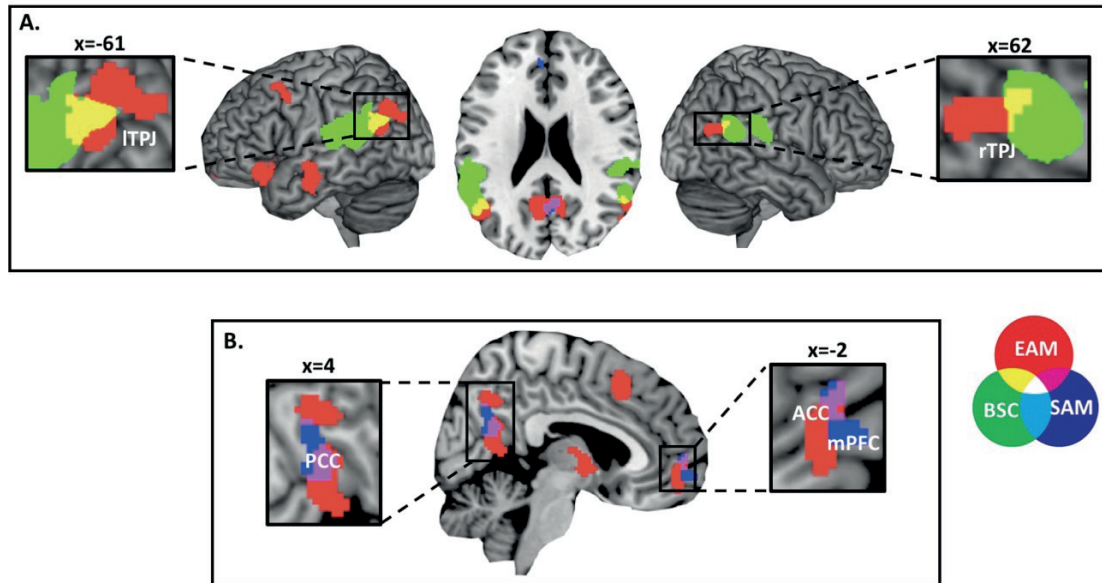


Figure 1A. Visualization of the anatomical overlap between BSC (Ionta et al., 2011) and EAM ALE analysis in bilateral parietal cortex. **Figure 1B.** Visualization of the anatomical overlap between SAM and EAM ALE analyses in the cortical midline structures. Within- cluster FWE-corrected $p < 0.05$ with $p < 0.001$ (uncorrected) as the cluster forming threshold. Label provided using the MRIcron.

4 Discussion

The present study extends previous EAM studies by investigating the role of subjective, conscious processing in autobiographical memory, based on spatial aspects of BSC (self-location and first-person perspective). Given the link of BSC with subjective experience and seminal proposals by Endel Tulving that subjective re-experiencing of specific past events is a fundamental component of EAM (Tulving, 1985, 2005), we speculated that neural processes related to multisensory bodily processing are not only relevant for BSC, but also for consciousness concerning past events and EAM (i.e. autonoetic consciousness). Subjective re-experiencing of own life events is often described as if experiencing the remembered event from a viewpoint and location that is similar to that during encoding of the event. Accordingly, we speculated that the first-person perspective and self-location of BSC are of particular relevance for autonoetic consciousness and EAM. The current data are preliminary (as we could only include data from (Ionta et al., 2011)), but allow to confirm this prediction. More brain imaging data on these two spatial aspects of BSC is needed to further confirm our findings.

Our findings suggest that EAM activity indeed anatomically overlaps with BSC in the AG. Previous work on BSC investigated self-related processing by using multisensory cues through a variety of experimental paradigms, highlighting contributions from own body signals

(Bergouignan et al., 2014; Blanke, 2012; Blanke et al., 2015; Blanke and Metzinger, 2009; Ehrsson, 2007; Serino et al., 2013; Tsakiris et al., 2010). We note that during the encoding of personal-life episodes, multisensory signals about the body of the observer that are of relevance for BSC are always perceptually co-present. Such signals are thus potentially of relevance for BSC and EAM, even though during encoding these signals often remain in the background. For instance, (Ciaramelli et al., 2010) found that patients with left-lateralized lesions in the posterior parietal cortex suffered from an impaired and disembodied, subjective experience associated with a navigation task. Moreover, Bergouignan et al. (2014) reported that recall of EAM items and hippocampal activity during the encoding of episodic events is modulated by the visual perspective from where the event was viewed during encoding. Using different methodology, St. Jacques et al. (2017) showed that first-versus third-person perspective during memory retrieval modulated recall of autobiographical events, and associated this with medial and lateral parietal activations. In a recent study (Bréchet et al., 2018b), VR technology has allowed us to experimentally control and manipulate key elements of BSC during EAM encoding and retrieval, revealing that classical BSC factors also influence EAM performance. Thus, our current findings are compatible with these data on shared resources for BSC and EAM and reveal an anatomical overlap bilaterally at the level of AG. However, many different manipulations of perspective and visual viewpoints have been carried out in the past (i.e. see Blanke, 2012). The subjective and behavioral changes as well as the associated brain activity as investigated for example by (Ionta et al., 2011) or St. Jacques et al. (2017) are thus not easily comparable. Thus, more work is also needed to investigate the common and distinct brain mechanisms involved in these different “perspective” manipulations.

Our finding is in line with previous neuropsychological and neuroimaging studies (Foster et al., 2015; Kim, 2016; Kim et al., 2012; Svoboda et al., 2006), consistently reporting the lateral parietal region as the second most frequently activated region outside MTL structures during EAM retrieval. Although the lateral parietal cortex has been often associated with visuo-spatial perception, attention (Corbetta and Shulman, 2002) and multisensory integration (Driver and Noesselt, 2008; Tomasino and Gremese, 2016), it is only more recently that studies associated the lateral parietal cortex and especially the AG with retrieval related to EAM (Bellana et al., 2017; Cabeza et al., 2007; Gilmore et al., 2015; Igelström and Graziano, 2017; Moscovitch et al., 2016; Rugg and Vilberg, 2013; Rutishauser et al., 2017; Sestieri et al., 2011, 2017). This has led to several suggestions about the contributions of the parietal cortex, especially AG, to EAM retrieval. For example, the working buffer hypothesis (Vilberg and Rugg, 2008) suggested different roles for the ventral and dorsal regions in lateral parietal cortex, linking ventral parietal cortex to EAM recollection (i.e. the ability to subjectively re-experience past events enabled by auto-noetic consciousness) and the dorsal parietal cortex to familiarity related processing (i.e. general

recognition of events without any details associated with noetic consciousness) (Cabeza et al., 2008). Recently, Bonnici et al. (2016) investigated the role of the AG during retrieval of unimodal and multimodal episodic and semantic memories. Their findings suggest that the AG may enable the multimodal (i.e. audio-visual) integration of sensory features into rich, vivid and subjectively relevant EAM. This interpretation of the essential role of AG in the subjective experiencing of multi-sensory past events is consistent with the recent research on BSC that highlighted the multi-sensory and sensorimotor processing and integration of different bodily stimuli to the sense of self localized in the lateral parietal area (i.e. Blanke et al., 2015). Nonetheless, the precise role of AG in memory and autobiographical memory is still a matter of controversy.

The current study revealed bilateral lateral posterior parietal activations in the AG (Brodmann area 39) for EAM, but not SAM. There is an increasing debate whether the neural correlates of EAM and SAM are shared or distinct. While Levine et al. (2004) claim distinct neural correlates for EAM and SAM, Renoult et al. (2012) suggest that the neural correlates of SAM may closely resemble episodic or semantic depending on the memory measures. Specifically, autobiographical fact and self-knowledge, which are heavily involved in self-referential processing, activate the MPFC. This finding is in line with a recent meta-analysis of Martinelli et al. (2013), which showed that SAM and conceptual self (CS) activated the medial prefrontal structures. Confirming our finding of ACC and PCC activity for SAM, recent meta-analyses that involved trait-judgements of the self vs. other or self vs. others events, suggested a critical role of anteromedial prefrontal cortex and posterior cingulate cortex in the self-referential processing (Kim, 2012; Northoff et al., 2006; Qin and Northoff, 2011). For example, the meta-analyses of Kim (2012, 2016) suggested that conscious memory retrieval, both semantic and episodic, is associated with the involvement of the intrinsic default mode network (DMN). Importantly, Piolino et al. (2009) emphasized that the lifelong changes in autobiographical memory play a critical role in the debate about the neural basis of EAM and SAM. Indeed, it is important to keep in mind the well-known temporal shift of autobiographical memories from episodic to semantic (Conway et al., 1997). This temporal shift corresponds to the concept of semantization of long-term memories over time (Brewer, 1986), which suggests that long-term autobiographical memories become a combination of both subjective experiences of EAM and self-knowledge and facts of SAM (Cabeza and St Jacques, 2007; Piolino et al., 2007; Westmacott and Moscovitch, 2003). Similarly, it is relevant to note the aspect of memory repetition, which also influences the autobiographical recollection. While re-living similar episodes (the so-called external repetition; for more detail see (Piolino et al., 2009) may lead to decontextualization of past events, thinking or talking about the past event (the so-called internal repetition) may enhance the details of the past events (Nadel et al., 2007; Rubin and Kozin, 1984). Renoult et al. (2012) suggested an intermediate category of declarative memory, the so-called personal semantics (i.e. autobiographical facts, such as “Jacob is the name of my brother”), which he compares to the general semantic knowledge about the world (such as “Jacob was the son of Isaac in the Old Testament). The authors pointed out that neuropsychological studies using Autobiographical Memory

Interview (AIM) of Kopelman et al. (1989) generally assume the same neural correlates of both personal and general semantics. Interestingly, several studies of Maguire and colleagues (Maguire and Frith, 2003; Maguire and Mummery, 1999) suggested an overlapping activity in medial prefrontal region for both personal and general semantics, however personal semantics showed stronger, left-lateralized activity in prefrontal cortex, retrosplenial cortex, temporal pole and temporoparietal junction. It is important to note that our current meta-analysis on SAM did not distinguish between studies investigating familiar, self-relevant semantic information (e.g., faces, places) and studies examining self-trait judgements. We highlight that our finding of CMS for SAM meta-analysis is similar to previous studies on self-referential processing, however we cannot exclude the possibility that separating the self-referential judgements as an independent meta-analysis could have led to further findings. The inclusion of incongruent studies is an important limitation of the present meta-analysis on autobiographical memory. Future work should specifically focus on particular aspects of episodic and semantic autobiographical memory, including the personal semantic and general semantic memory and also improve the analysis with respect to BSC.

Tulving (1972) theoretically differentiated two main components of autobiographical memory by their distinct states of consciousness. SAM has been characterized by the noetic consciousness (i.e. subjects remember personally relevant facts) (Schacter et al., 2007; Tulving, 2002). Contrary, auto-noetic consciousness defines the EAM (i.e. subjects re-experience the past or project themselves into the future) (Tulving, 1972). Based on the evidence that both EAM and BSC recruit the lateral parietal cortex and given the fundamental link between BSC and EAM with multimodal subjective, conscious experiences, we hypothesized that there would be an anatomical overlap in this structure between BSC and autobiographical memory, specifically for the episodic (EAM), but not the semantic aspects (SAM). The present study confirms and extends previous EAM studies, by showing that the neural processes related to multisensory bodily processing are not only relevant for BSC, but also for consciousness concerning past events and EAM (i.e. auto-noetic consciousness). Thus, the present ALE data on EAM and SAM corroborate the recent proposals about the involvement of the lateral parietal cortex, including the AG and adjacent regions of the superior temporal gyrus in EAM. Accumulating evidence points toward the causal role of AG in the subjective, conscious recollection of past episodes. The current findings are thus consistent with the proposal that particularly the AG and not the cortical midline structures that are involved in the self-referential processing, is involved in integrating multiple memory features into a multi-modal (i.e. including sounds, smells, sights) conscious representation that enables the rich and vivid subjective re-living of an event.

The present data suggest that AG (revealed by the study of Ionta et al. (2011) was jointly involved in BSC and EAM. Unlike neurological patients with damage to MTL structures (Scoville, 1957; Steinworth et al., 2005), patients with lateral parietal lobe damage do not suffer from severe EAM deficits. For this reason, the subtler EAM impairments associated with

damage to the lateral parietal cortex were previously largely overlooked. However, recent clinical studies investigating memory in patients with parietal lesions have provided valuable insights and especially highlighted contributions of the AG to EAM (Berryhill et al., 2007; Hower et al., 2014; Simons et al., 2010). Even though patients with damage to parietal cortex are able to retrieve past personal events, a number of such lesion studies revealed that the ventral part of the lateral parietal cortex, especially the left AG, is associated with the impairment of subjective re-experiencing of vivid, rich and multi-sensory EAM. Moreover, patients with parietal lobe damage often report lower confidence in the retrieval of their EAM. These findings suggest a particular role of AG in the subjective experience of EAM recollection and indicate that the MTL may not be sufficient for the full-blown subjective experience of the self in the past. Critically, it is important to mention a number of neuroimaging studies that have described the functional differentiation on the level of neural networks, which play a role in episodic memory retrieval, particularly the MTL structures and frontoparietal regions. These neuroimaging studies demonstrated that an activation within these latter brain circuits often reflects the memory recollection versus the subjective feeling of familiarity related to the contextual memory details (Eichenbaum et al., 2007; Rugg and Vilberg, 2013; Squire et al., 2004). This functional heterogeneity within parietal regions and between the sub-regions of MTL activity patterns supports the different aspects of autobiographical memory. For example, in the recent study of Brown et al. (2018), participants were asked to judge the temporal sequence of past events from their own life or lives of others. While activity in most of the MTL regions was related to episodic autobiographical memory, neural activity in superior parietal lobule, intraparietal sulcus and hippocampal tail showed similar involvement for both episodic and semantic autobiographical memories. Importantly, activity in the angular gyrus revealed a graded pattern from episodic recollection to semantic remembering. Furthermore, several neuroimaging studies (Addis et al., 2004b, 2004a; Holland et al., 2011; Levine et al., 2004) showed enhanced activity in the left parahippocampus, left temporoparietal junction, fusiform gyri and right inferior temporal cortex when past events are repeated compared to unique events. Recently, Jonker et al. (2018) developed a paradigm during which participants encoded object-scene pairs, following with retrieval resulting in increased re-activation of both target objects and contextually related objects in a network including the hippocampus and posterior medial network of parietal regions, known as the default mode network (Ranganath and Ritchey, 2012; Rugg and Vilberg, 2013). Based on the present meta-analytical findings we suggest that BSC-related processing in bilateral AG may play an important role in EAM, especially with respect to subjective re-experiencing of EAM. However, it is important to highlight that this anatomical overlap between EAM and

BSC is small and both cognitive functions have a largely separated basis. Furthermore, an important limitation of the present study is we could only include a single neuroimaging study that experimentally investigated self-location and first-person perspective. Future work will hopefully be able to perform meta-analysis also for these BSC components, thereby improving the analysis with respect to EAM, as well as with other forms of perspective manipulations relying on viewpoint changes or mental imagery.

Conclusion

Recent data in cognitive neuroscience suggest that the lateral parietal cortex contributes to the EAM retrieval. The present study extends earlier neuroimaging and neuropsychological patient work and provides preliminary evidence for shared neural parietal resources between BSC and EAM, but not SAM. The present data suggest that conscious re-experiencing of past life episodes (EAM) and the conscious on-line experience of being located and experiencing the world first-person (BSC) both depend on the lateral parietal cortex structures. We find that especially the AG is jointly involved bilaterally in processing related to BSC and EAM and may be a key structure for neural processing related to self-consciousness including conscious online experiencing and later re-experiencing in EAM.

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Reference	Contrast	Imaging method	Number of foci	Number of participants
Addis et al. (2004a)	specific and generic EAM vs semantic control task	fMRI	16	14
Addis et al. (2004b)	specific and generic EAM vs semantic control task	fMRI	54	14
Addis et al. (2012)	EAM vs semantic and visuospatial control tasks	fMRI	18	15
Botzung et al. (2008b)	EAM vs SM	fMRI	34	10
Cabeza et al. (2004)	EAM and lab retrievals	fMRI	10	13
Conway et al. (1999)	recent and remote EAM vs cued recall of paired associates	PET	11	6
Daselaar et al. (2008)	EAM access and elaboration	fMRI	20	17
Denkova et al. (2006a)	EAM vs SM	fMRI	26	10
Denkova et al. (2006b)	EAM vs SM	fMRI	25	20
Donix et al. (2010b)	recent and remote EAM vs recent and remote SM	fMRI	26	15
Fink et al. (1996)	EAM vs rest and impersonal task	fMRI	9	7
Gardini et al. (2006)	EAM vs baseline	fMRI	20	14
Gilboa et al. (2004)	EAM vs semantic control task	fMRI	22	9
Greenberg et al. (2005)	EAM vs semantic control task	fMRI	18	16
Hennessey Ford et al. (2011)	EAM vs semantic control task	fMRI	21	16
Holland et al. (2011)	EAM vs semantic control task	fMRI	9	31
Hoscheidt et al. (2010)	EAM vs description of music with adjectives	fMRI	27	17
Levine et al. (2004)	personal episodic memories vs personal semantic	fMRI	20	5
Maguire et al. (1999)	personal episodic memories vs non personal memories	PET	9	8
Maguire et al. (2003a)	EAM vs control task	fMRI	10	24
Maguire et al. (2003b)	personal episodic memory vs public event control task	fMRI	6	24
Mayes et al. (2004)	EAM vs semantic control task	fMRI	14	9
Milton et al. (2011)	remember vs new responses	fMRI	36	15
Nadel et al. (2007)	remote and recent EAM vs rest	fMRI	16	12
Oddo et al. (2010)	remote and recent EAM vs SM	fMRI	14	15
Okuda et al. (2003)	EAM vs baseline	fMRI	18	12
Piefke et al. (2003)	EAM vs baseline	fMRI	18	20
Piolino et al. (2008)	EAM vs semantic control	fMRI	19	12
Rabin et al. (2009)	vivid EAM and Tom vs baseline	fMRI	20	20
Ryan et al. (2001)	EAM vs semantic control task	fMRI	22	7
Söderlung et al. (2012)	EAM vs odd/even number judgement	fMRI	19	12
St Jacques et al. (2011)	EAM access and elaboration	fMRI	28	17
St Jacques et al. (2011)	EAM access and elaboration	fMRI	15	17
St Jacques et al. (2012)	self projection of one's own self	fMRI	13	23
Summerfield et al. (2009)	real EAM vs imagined EAM	fMRI	12	18
Svoboda et al. (2009)	EAM vs general semantic memory	fMRI	19	11
Trinkler et al. (2009)	recognition task	fMRI	25	14
Tsukura et al. (2002)	recall of personal events vs retrieval of lexical meaning of words	fMRI	26	9
Vanderkerchove et al. (2005)	EAM vs rest	fMRI	16	16
Viard et al. (2007)	EAM vs low level baseline conditions (i.e. pseudowords)	fMRI	24	12
Viard et al. (2011)	EAM vs low level baseline conditions (i.e. pseudowords)	fMRI	28	12

Supplementary Table 1. Overview of studies investigating neural correlates of episodic autobiographical memory (EAM).

fMRI= functional magnetic resonance

PET= positron emission tomography

Reference	Contrast	Imaging method	Number of foci	Number of participants
Addis et al. (2004a)	SAM vs EAM	fMRI	3	14
Donix et al. (2010a)	familiar faces + places vs unknown faces and places	fMRI	16	12
Gobbini et al. (2004)	familiar faces vs unfamiliar faces	fMRI	19	10
Leibenluft et al. (2004)	familiar faces vs unfamiliar faces	fMRI	36	7
Levine et al. (2004)	SAM vs EAM	fMRI	21	5
Maddock et al. (2001)	familiar names vs unfamiliar names	fMRI	24	8
Maguire et al. (2003a)	SAM vs control	fMRI	17	12
Nakamura et al. (2000)	(familiar faces - control) vs familiar places - control)	PET	6	7
Shah et al. (2001)	familiar faces and voices vs unfamiliar faces and voices	fMRI	2	10
Sugiura et al. (2005)	familiar objects and places vs unfamiliar objects	fMRI	7	25
Sugiura et al. (2006)	familiar names vs unfamiliar names	fMRI	47	24
Sugiura et al. (2009)	familiar names vs unfamiliar names	fMRI	7	28
Sugiura et al. (2011)	familiar faces vs unfamiliar faces	fMRI	9	24
D'argembeau et al. (2008)	self trait judgement vs other traits judgement	fMRI	8	16
Gutchess et al. (2007)	self trait judgement vs other traits judgement	fMRI	9	19
Heatherton et al. (2006)	self trait judgement vs other traits judgement	fMRI	9	30
Jenkins et al. (2008)	self-opinion vs other-opinion	fMRI	1	13
Kelley et al. (2002)	self trait judgement vs other traits judgement	fMRI	2	24
Kjaer et al. (2002)	self trait judgement vs other traits judgement	PET	16	7
Modinos et al. (2009)	self trait judgement vs other traits judgement	fMRI	11	16
Oschner et al. (2005)	self trait judgement vs other traits judgement	fMRI	6	16
Pfeifer et al. (2007)	self trait judgement vs other traits judgement	fMRI	25	12
Schmitz et al. (2004)	self trait judgement vs other traits judgement	fMRI	6	19
Seger et al. (2004)	self trait judgement vs other traits judgement	fMRI	4	12
Zhu et al. (2007)	self trait judgement vs other traits judgement	fMRI	3	26

Supplementary Table 2. Overview of studies investigating neural correlates of semantic autobiographical memory (SAM).

fMRI= functional magnetic resonance

PET= positron emission tomography

2.3 Study 3

The bodily-self retroactively and selectively strengthens episodic memory

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Abstract

Memory is an adaptive process that continuously updates itself, according to what information may be important to oneself in the future. Recently, it has been demonstrated that memory for older, neutral images can be selectively and retroactively enhanced by future emotional (fearful or rewarding) events, which are conceptually related to the neutral images, while unrelated events encoded at the same time did not profit from the retroactive strengthening. Personally meaningful past episodes, defined as episodic autobiographical memories (EAM), are related to our sense of bodily-self, the so-called bodily self-consciousness (BSC). We here hypothesized that the presence of the bodily-self in previously neutral scenes is a strong, salient stimulus that would retroactively strengthen the memory for these past episodes. We therefore used an immersive virtual reality (VR) system to test whether the presence of one's own physical body can retroactively and selectively strengthen EAM. Our technology enabled us to study and demonstrate that the presence of one's own physical body creates a strong retroactive effect and selectively strengthens EAM. First, we extend our recent findings by showing that the presence of congruent multisensory, visual and proprioceptive cues from one's own physical body experimentally enhances EAM performance. Second, we demonstrate that these salient, bodily self-related cues can selectively and retroactively modify post-encoding memory consolidation. Our findings bring a new evidence that personally meaningful memories are not fixed, but may be weakened as well as strengthened by later self-relevant events, which is of relevance for the understanding of memory disorders.

Keywords: episodic autobiographical memory, bodily self-consciousness, post-encoding consolidation, behavioral tagging, real-life events

Introduction

Most events that we experience during our daily life will be forgotten ^{1,2}. We form detailed and lasting memories only for a small part of our daily experiences. What determines which of the everyday experiences will be remembered? Past events that are personally meaningful and related to our sense of self tend to form into our episodic autobiographical memories (EAM) ³. EAM comprises precise information about the place, the time as well as the content of a self-relevant, past event. We tend to remember salient past events, because the information may be relevant to us in the future. However, we do not always know when an important event will happen. In fact, many seemingly irrelevant life events may become important only with hindsight. For example, that stranger who asked for directions become more relevant after you realize that your wallet is missing. Synaptic and behavioral tagging hypotheses have suggested a neurobiological mechanism of memory consolidation, by which initially unstable and weak memories are retroactively strengthened by conceptually related strong event ⁴⁻⁸. It is crucial to temporarily store apparently irrelevant events in memory, in case these unimportant past events may gain unexpected importance later in time. Thus, these hypotheses suggest that initially weak memories may become strengthened, if these memories gain meaning later in time.

Every event in our lives is encoded from the natural perspective of our own bodies (first-person perspective, 1PP) ^{9,10}. Subjective re-experiencing of personal, past events is often described as from a viewpoint and location that is similar to that during encoding of the event. The conscious awareness of the self is intrinsically linked to the processing of multisensory bodily signals ¹¹⁻¹³. The subjective feeling that our body belongs to us (self-identification) and is placed at a particular position (self-location) belong to the fundamental aspects of bodily self-consciousness (BSC) ^{12,14}. In our recent study ¹⁵, we have examined the influence of congruent multisensory, visual and proprioceptive cues on episodic autobiographical memory. Crucially, this study showed that memory performance was significantly enhanced when participants viewed their body immersed in the virtual reality (VR) scenes during encoding, thus linking the sense of self and the bodily self-consciousness particularly to episodic autobiographical memory. This immersive VR technology, which provides a fully controlled, yet real life-like, self-relevant multisensory and contextually rich event, may be especially beneficial for the understanding of enhancements or impairments of self-relevant, personal episodic memory.

Recently, two behavioral studies demonstrated how memory for neutral images can be enhanced by future fearful ¹⁶ or rewarding ¹⁷ events, which were conceptually related to the neutral images. Consistently with the tag and capture mechanism ⁴, authors hypothesized that a weak synaptic tag may have been activated during a first phase, the so-called “pre-conditioning classification” of an incidental memory encoding. During the pre-conditioning classification, two neutral categories of images depicting animals and tools appeared to be of the same relevance. However, during a second phase of the incidental encoding, the so-called “conditioning classification”, a salient event, either fear conditioning or reward motivation, became associated with only one of the two categories of images. This association between a group of neutral images and salient event might have triggered selective protein-synthesis consolidation of the previously weak memory trace ⁴. As a result, during a later memory recognition task, participants remembered not only objects that were associated with fear or reward during the conditioning phase, but surprisingly they also remembered better the conceptually-related images from the pre-conditioning phase. Interestingly, the retroactive memory enhancement was not only category selective, but also time-dependent. Memory was strengthened with delay (24h or 6h), but not immediately after encoding, indicating that such form of memory consolidation required post-encoding long-term mechanisms ^{18–20}. Although these two behavioral studies provided a new evidence that meaningful events may selectively consolidate memory for prior, seemingly insignificant information at the time of encoding, some important questions remain open. These studies demonstrated that re-prioritization, i.e. memory is retained if an information becomes relevant, occurs under fear conditioning ¹⁶ and when associated with a reward motivation ¹⁷. However, it remains unknown, whether this retroactively enhancing effect could be triggered with different type of salient events, such as the presence of one’s own physical body. In addition, previous studies used lab-based images of animals or tools presented on the computer screen to test the retroactive strengthening of episodic memory. Critically, it is not known whether retroactive strengthening would extend to more realistic and natural situations of past experiences. Using immersive VR technology that allows to test episodic autobiographical memory in a fully controlled setting may be particularly valuable for the understanding of personally meaningful, enhancing or impairing effects on memory.

In a previous VR study ¹⁵, we showed that bodily self-relevant information at the encoding strengthens later memory for real-life events, thereby associating the bodily self-consciousness and one’s sense of self to episodic autobiographical memory. Here we tested whether bodily self-relevant cues, similar to the emotionally relevant cues, could retroactively enhance

previously encoded weak, neutral memories. Our main goal was thus to test whether the physical body selectively and retroactively strengthens the memory for contextual details of real life-like events. In order to test the selectivity of the retroactive memory strengthening, we used inside rooms and outside scenes as two distinct categories of events and tested whether the body-effect is category specific (experiment 2). We hypothesized that a.) the presence of one's own physical body would retroactively enhance memory for real life-like events and that b.) the retroactive memory enhancing would be selective to conceptually related items (e.g., body-present condition in inside rooms would enhance prior memory of inside rooms, but not outside scenes), while unrelated items encoded (memory for outside scenes) at the same time would not benefit from the retroactive memory strengthening and vice versa. To test these two hypotheses, we used the Reality Substitution technology (RealiSM), a novel form of mixed virtual and augmented reality. As in our previous study ¹⁵, this VR technology allowed us to present real-life episodes and manipulate particular details in them. We were able to immerse and manipulate the presence or absence of the participants' physical bodies in the inside rooms and outside scenes, so that they felt as if they were present in there. Thus, our technology enabled us to further examine the link between self-processes in BSC and EAM by immersing participants into contextually rich, inside rooms and outside scenes (similar to encoding animals and tools in the previous two studies ^{16,17}). Instead of using fear conditioning or reward, we associated one of the two conditions (i.e. rooms or scenes) with a presence or absence of one's own physical body.

Prior to testing our key hypothesis that the memory enhancing, bodily self-related effect is category specific, we had to create VR compatible inside rooms and outside scenes as two distinct categories of events (similar to animals and tools). For this, we followed-up on our prior study ¹⁵ in which we used inside rooms and showed that the presence of one's own physical body enhanced the memory for real-life like events of those inside room. Here, we expanded the experimental setting to new paradigms consisting of outside scenes (experiment 1), into which were participants immersed during two stages (encoding and retrieval) of EAM testing. We hypothesized that the memory for contextual details of the outside scenes (similar to inside rooms) and the subjective confidence in one-hour delay memory recognition task would increase in the body-present compared to body-absent condition.

Results

Experiment 1: Body x nobody condition

In order to assess the enhancement of memory for real-life like events based on the presence or absence of one's own physical body, participants were immersed into 2 outside scenes (similar to previous study with inside rooms) that were pre-recorded and played via a head mounted display (HMD). To familiarize with the VR technology, each participant was immersed into a scene for 5 minutes. We specifically asked the participants to remain seated, turn and look around and to explore the environment. The experiment consisted of 2 sessions, an incidental encoding task (session 1) followed by one-hour delayed surprise memory recognition task (session 2). The design and procedure are depicted in **Figure 1**.

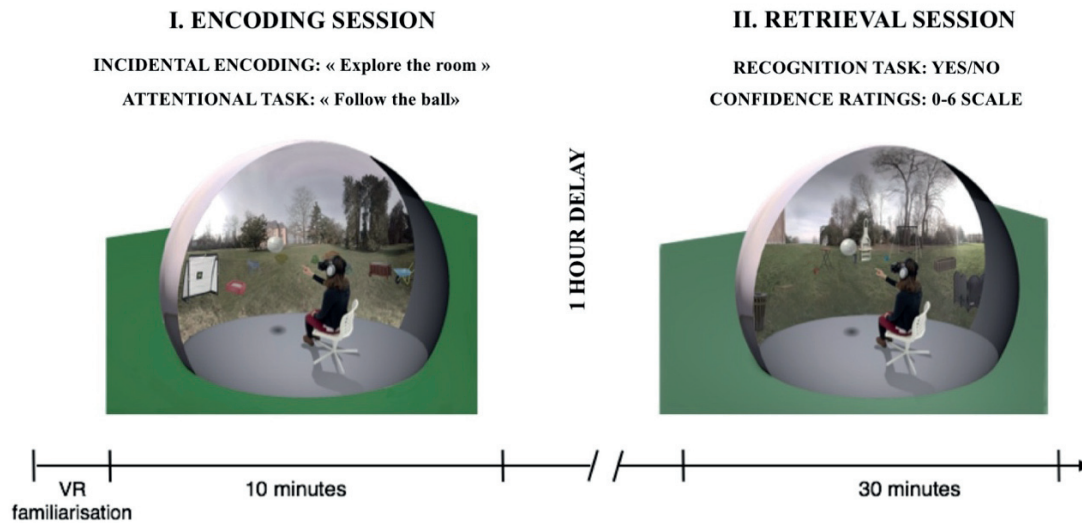


Figure 1: Study paradigm of experiment 1. First, participants incidentally learned the context of two different outside scenes (i.e. encoding session; 10min). Participants were immersed back into the scenes with one-hour delay and were asked to perform a recognition task together with subjective confidence ratings for each presented scene (i.e. retrieval session; 30 min). Before the actual study, participants were seated in a chair, they were asked to put on the HMD and noise-cancelling headphones to avoid external disturbances and familiarised themselves with the VR technology (10min).

The main manipulation (i.e. the presence or absence of one's physical body) was accomplished with the use of the stereoscopic depths cameras (i.e. turning them on/off) to capture in real-time participants' bodies from the 1PP. In one scene, participants could see their physical hand, trunk and legs, hence there was a visual feedback of the physical body (i.e. the stereoscopic depths cameras were turned on) (**Figure 2a**). In the second scene, there was no visual feedback of subject's body (i.e. the stereoscopic depths cameras were turned off) (**Figure 2b**). The order of presentation of the body and nobody condition was counterbalanced between participants.



Figure 2: An example of physical bodily-self manipulation in the pre-recorded outside scene. Participants were asked to point with their finger at the moving ball. **2a.** Participants experienced the feeling of being physically present in the outside scene as they had the visual feedback of seeing their physical hand. **2b.** Participants were physically pointing at the ball, but there was no visual feedback.

10 daily-life objects, such as a flowerpot or a bench in a park, were positioned in both scenes during the memory encoding session (session 1). Each scene included different set of 10 objects in order to keep the same level of novelty and to avoid any facilitation on the following recognition task. During the memory retrieval session (session 2), scenes stayed either exactly the same as during encoding (i.e. the same positioned 10 daily-life objects) or some of the objects (i.e. 1, 2 or 3 objects) were replaced by new objects. In total, 20 objects were presented in the 2 outside scene.

In order to examine whether objective memory performance ratings differed depending on the body x nobody condition for hit rate and confidence hit, statistical analysis relied on a paired t-test. During the one-hour delayed condition, participants showed a significantly higher hit rate in the body condition ($M = 77.8$, $SEM = 5.0$) than in the nobody condition ($M = 59.2$, $SEM = 9.4$); $t(13) = 2.4$, $p = 0.02$ (**Figure 3a**). These data show that participants had greater objective EAM performance in the one-hour delayed condition for outside scenes when tested with their body present than absent during initial memory encoding. Interestingly, the subjective confidence ratings for hits in the body group ($M = 4.9$, $SEM = 0.2$) were not significantly different from the nobody group ($M = 4.2$, $SEM = 0.4$); $t(13) = 1.7$, $p = 0.1$ (**Figure 3b**). Similarly, to examine the false alarm rate and confidence false alarm for subjective confidence ratings depending on the body x nobody condition, a paired t-test was performed. False alarm rates did not differ between both groups (body group: $M = 25.4$, $SEM = 3.5$; nobody group: $M = 20.0$, $SEM = 3.0$; $t(13) = 1.0$, $p = 0.2$) (**Figure 3c**). However, participants were subjectively more confident when making false alarms in the body group ($M = 4.5$, $SEM = 0.2$) than in the nobody group ($M = 3.8$, $SEM = 0.3$); $t(13) = 2.1$, $p = 0.05$ (**Figure 3b**). These results show that both the objective EAM as well as the subjective confidence for false alarms increased in the body condition.

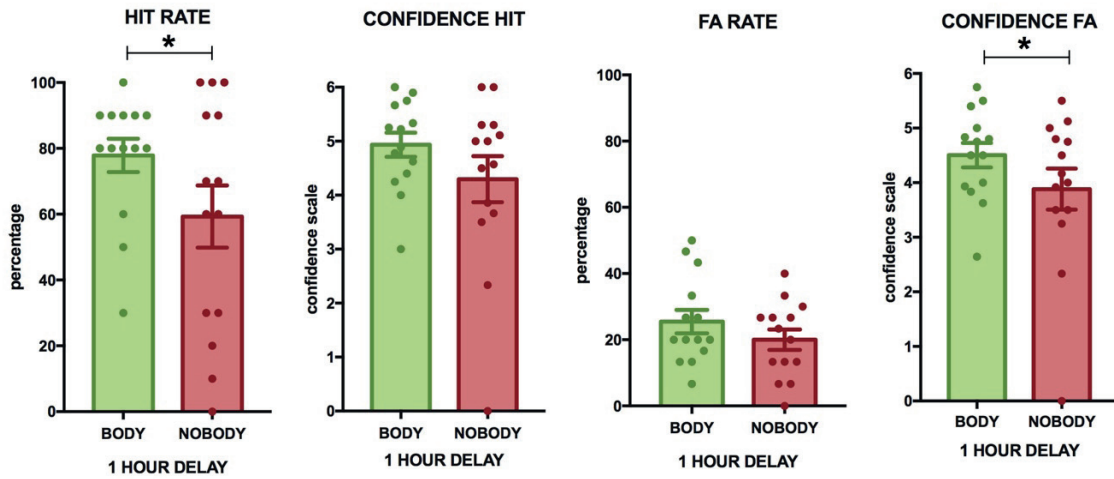


Figure 3: EAM performance in experiment 1 (body x nobody, one-hour delay memory recognition task). EAM performance (hit rate, false alarm rates) and subjective confidence ratings are indicated in percentage + SEM. (**) $P < 0.01$; (*) $P < 0.05$. **3a.** Hit Rate; **3b.** Confidence ratings (Hits); **3c.** False Alarm Rate; **3d.** Confidence ratings (False alarms).

In order to test the effects of the body condition (i.e. body present x body absent) and the number of objects changed (i.e. 1 object, 2 objects or 3 objects) on the false alarm rates and on the confidence for the false alarms, 2 x 3 repeated measures ANOVA was performed. This analysis was thus conducted on false alarm rates as by definition no objects changed for hits. The results revealed a statistically significant main effect for the objects changed $F(2, 26) = 0.8$, $p < 0.0005$, partial $\eta^2 = 0.6$ (**Figure 4a**). Pairwise comparisons were performed for statistically significant main effects and revealed that participants made progressively fewer false alarms with increasing number of objects (all p -values < 0.0005). We conclude that the number of false alarms decrease with increasing number of replaced old objects for new ones compared to the original encoding stage. Likewise, we tested whether the subjective confidence in the performance accuracy (i.e. confidence ratings for false alarms trials) depended on the number of objects changed (i.e. 1 object, 2 objects, 3 objects) within each scene and on the one hour delayed performance. There was a statistically significant main effect for objects changed $F(2, 26) = 10.3$, $p = 0.006$, partial $\eta^2 = 0.4$. Post-hoc analysis revealed a statistically significant change from 1 object to 3 objects ($p < 0.03$; Bonferroni corrected) (**Figure 4b**). These data suggest that the number of false alarms as well as the subjective confidence for number of false alarms decrease with an increasing number of replaced old objects for new ones.

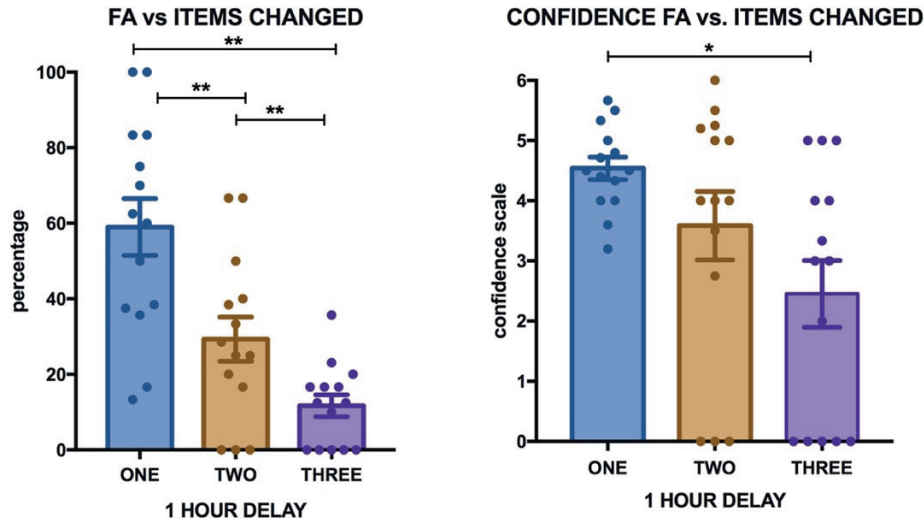


Figure 4: False Alarm versus Number of Objects Changed (i.e. 1 item, 2 objects, 3 objects). EAM performance is indicated in percentage + SEM are indicated. (**) $P < 0.01$; (*) $P < 0.05$. **4a.** False Alarm versus Number of Objects changed **4b.** Confidence Rate for False Alarm versus Number of Objects changed.

In this first experiment, we thus demonstrate that the presence of congruent multisensory cues from one's body experimentally enhances the objective EAM performance. This finding expands our previous paradigm of inside rooms¹⁵, by showing here that the embodied-self modifies the objective recollection of every-day like EAM using our novel outside scenes. Several VR paradigms have been used in the research on embodiment (for a review, see¹²) and showed BSC can be modulated by showing the body or body parts of the participant from different first-person viewpoints compared to showing no body at all. Here, we extend this BSC principle to memory research by showing that the recognition of real life-like scenes that included the subject's body (as is characteristic of normal everyday perception) was modulated and significantly enhanced with respect to the same scenes without such a bodily view.

Experiment 2: Retroactive Strengthening

In order to investigate whether the physical body selectively and retroactively strengthens the memory for contextual details of real life-like events, participants were immersed into distinct rooms and scenes. Our aim was to examine whether bodily cues would retroactively boost previously encoded neutral memories. The encoding task (session 1) had two phases: the pre-body phase (phase 1) and body vs. nobody phase (phase 2). Importantly, to avoid any potential rehearsal effect, participants were not instructed to memorize (incidental encoding), followed by a one-hour delayed surprise memory recognition task (session 2) (**Figure 5**). During "the pre-body phase" (phase 1), 2 inside rooms and 2 outside scenes were presented each with 10

daily-life objects (e.g., table, painting in the inside rooms; bike, barbecue grill in the outside scenes). Objects were presented one at a time, each placed in a different position. The pre-body phase (phase 1) was similar to the “pre-conditioning classification task” (phase 1) of an incidental memory encoding in the two previous selectively and retroactively strengthening memory studies ^{16,17}. During “the body x nobody phase” (phase 2), 2 new inside rooms and 2 new outside scenes were presented each with 10 novel daily-life objects (e.g., lamp, candle stand in the inside rooms; balloon, garden playhouse in the outside scenes) one at the time. Participants were asked to find the object and physically point at it. The body x nobody phase (phase 2) was similar to the “conditioning classification task” (phase 2) of an incidental memory encoding in the two previous studies ^{16,17}. In the previous studies, a salient event (fear or reward) applied during phase 2 became associated with only one of the two categories (tools or animals) of images. In our current study, we have substituted the fear conditioning or reward motivation with the presence or the absence of one’s own physical body and used inside and outside rooms as the two testing categories. During the memory retrieval stage, all 4 inside rooms and 4 outside scenes were presented again with total of 40 old objects (seen during phase 1 and phase 2 of encoding) and 40 new objects per each room or per each scene, serving as distractors. Each object was presented one at a time.

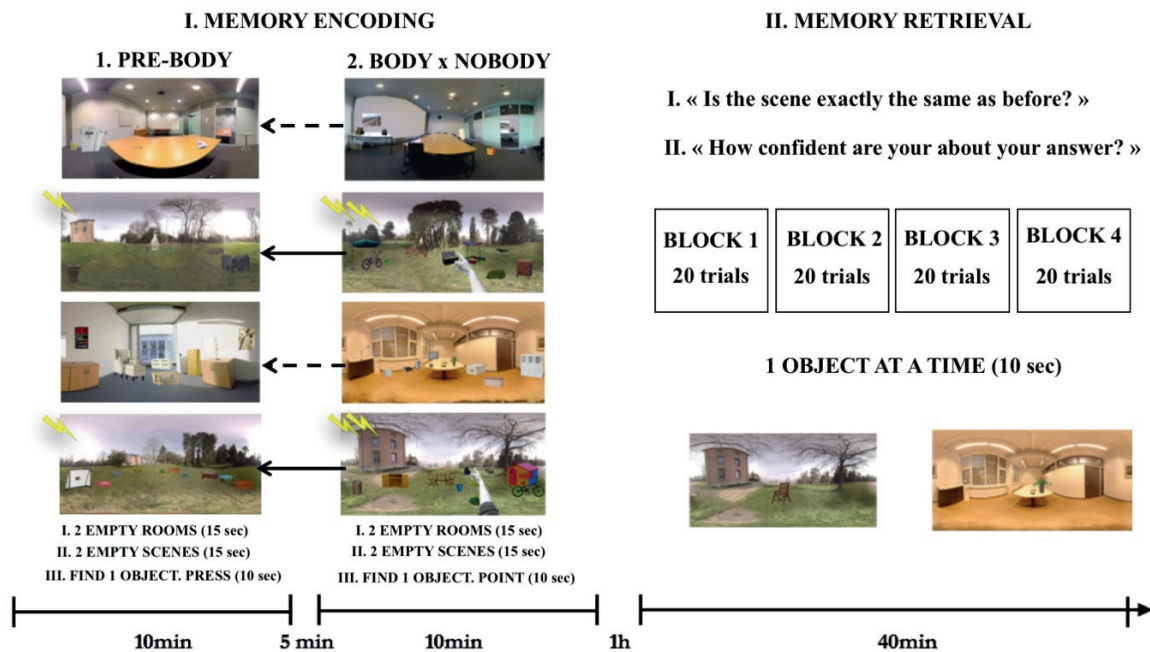


Figure 5: Study paradigm of experiment 2. First, participants explored 2 empty rooms and 2 empty scenes without any object for 15sec each. Participants were then instructed to find daily-life objects (40 total) belonging to inside rooms (20 objects) and outside scenes (20 objects) and press a button once they found it during the pre-body conditioning (phase1). During the body x nobody condition (phase 2), participants explored 2 new empty rooms and 2 new empty scenes without any object for 15sec each. Participants were then instructed to find new set of daily-life objects (40 total) belonging to inside rooms (20 objects) and outside scenes (20 objects) and point toward the object once they found it. During the memory retrieval, participants were asked to recognize each object as new/old and rate how confident

they are about the answer.

In order to test the effects of the body condition (i.e. body present vs. body absent) and the phase (pre-body condition vs. body x nobody condition) on the memory for contextual details of real life-like events, repeated measures ANOVA was performed. Follow-up t-test were conducted separately for each phase (phase 1 and phase 2). Where appropriate, Greenhouse-Geisser corrections of degrees of freedom were used. Significant ANOVA effects were explored by post-hoc tests using Bonferroni correction. The significant level was set to alpha 0.05. A significant main effect of body condition (i.e. body x nobody) was found in the retroactive, one-hour delayed group for contextual details of real life-like events. $F(1, 14) = 0.8, p < 0.0005, \text{partial } \eta^2 = 0.6$. As predicted from results of Experiment 1 and our previous study¹⁵, a memory enhancement was also found in the body condition ($M = 55.0, \text{SEM} = 3.5$) x nobody condition ($M = 46.3, \text{SEM} = 3.3$) for items shown in phase 2 ($t(14) = 2.4, p = 0.02$) (**Figure 6b**). More importantly, the body effect on memory extended retroactively for the conceptually related objects that were observed in the pre-body condition (phase 1), even if the body was not shown at that phase. Specifically, the follow up t-tests revealed that EAM performance for the hit rate was higher in the pre-body ($M = 57.6, \text{SEM} = 3.1$) as compared to the pre-nobody condition ($M = 49.5, \text{SEM} = 3.6$); ($t(14) = 2.22, p = 0.04$) (**Figure 6a**). These results suggest that weak memories from the pre-body phase once conceptually related acquired salient relevance.

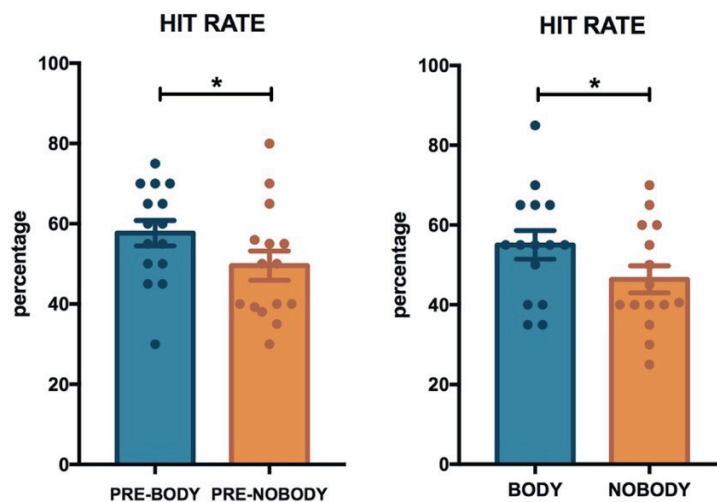


Figure 6: EAM performance in experiment 2 (one-hour delay memory retrieval). EAM performance (hit rate) is indicated in percentage + SEM. (**) $P < 0.01$; (*) $P < 0.05$. **6a.** Pre-conditioning/pre-body hit rate (phase 1); **6b.** Body x nobody Hit rate (phase 2).

Our findings bring a new evidence for retroactive memory enhancement, showing that also multisensory bodily self-related cues can significantly modify post-encoding memory consolidation. This finding confirms and extends the findings of previous studies^{16,17} by showing that a.) the presence of one's own

physical body does retroactive enhance memory for real life-like events and that b.) the retroactive memory enhancing is specific to conceptually related items encoded in real life-like scenes.

Discussion

In two experiments, we explored the relationship between multisensory bodily cues and memory recollection for contextual information. The main finding (experiment 2) is that memory for seemingly insignificant every-day details of neutral real life-like events can be enhanced, if future conceptually related details acquire salience by the presence of one's own physical body. Recent behavioral studies ^{16,17} showed that emotional learning (aversive as well as appetitive) can retroactively and selectively strengthen memories for conceptually related neutral events. However, unlike in the previous lab-based episodic memory studies, we used our VR technology, which a.) enabled us to immerse our participants and their physical bodies into complex real-life inside rooms and outside scenes, thus creating the subjective feeling of being physically present in there and b.) experimentally control both stages of memory encoding and retrieval and manipulate the presence or absence of participants' own physical bodies in the real-life like events. Here, we provide an experimental evidence that the memory for real life-like events may be explicitly manipulated by the self-related, bodily cues. In this study, we argue that the experience of the physical bodily-self is intrinsically linked to the autobiographical-self as we show that the memory for episodic details gets enhanced in the body-present condition compared to the body-absent condition. Furthermore, the effect of the bodily-self retroactively and selectively boosts initially weak memories as compared to no enhancement of the bodily-absent effect.

Our findings suggest that the self-relevant, episodic memories and self-related, multisensory processing underlying the BSC are intimately linked together. Here, we argue that the fundamental aspect underlying both EAM and BSC is the autonoetic consciousness, the subjective human ability to mentally travel in time and re-experience self-relevant events ²¹. Previous lines of research succeeded in experimentally manipulating multisensory bodily stimuli to induce changes in distinct components of BSC, including self-identification (the experience of identifying with one's body), self-location (the experience of where I am in space) and 1PP (the experience of from where do I perceive the world) ^{11,12}. For instance, tactile stimulation of a subject's hand or body coupled with spatially and temporally synchronous stroking of a viewed virtual hand or body gives rise to illusory self-identification and illusory self-location over a virtual body ²²⁻²⁴. Here, and in our previous study ¹⁵, we demonstrated that

multisensory bodily cues – in this case the presence and the congruency of body cues with body movements in VR – affect higher-level cognitive processes related to the self, such as EAM.

The current study makes a step further in linking BSC and EAM. Our findings reveal that bodily cues enhance retroactively memory for previously encoded episodic events. Memory consolidation is a dynamic process by which an experience is transformed into a long-term memory^{20,25–27}. What determines which memories may last, while others fade? While we may not consciously remember all the insignificant details of our every-day lives, we tend to remember those details of past events, which may become useful for predicting and controlling important events in the future²⁸. Yet, it seems to be relevant to temporarily store inconsequential details of events, in case these details may gain saliency later in time. The study of Frey and Morris⁴ provided a neurobiological mechanism that suggests that initially weak and unstable memories are tagged for later stabilization by long-term potentiation (LTP) processes. This neurobiological mechanism has been extended to show how weak training of rats, which would be forgotten, may be stored in long-term memory after a novel behavioral experience, the so-called behavioral tagging^{6,29,30}. However, whether the behavioral tagging also occurs in humans was unknown until the recent behavioral studies^{16,17}. These studies demonstrated that only specific, older events that were conceptually related to following salient experiences, become selectively enhanced while other older, unrelated information that was encoded at the same time did not benefit from the retroactive strengthening. This effect was found only with delay, but not immediately after the encoding, which suggest the importance of post-encoding consolidation processes. Studies of post-encoding consolidation suggest that various processes may predict better memory performance. For example, memory performance has been shown to correlate with experience dependent hippocampal-cortical functional connectivity¹⁸, persistence of multi-voxel patterns into rest and active task³¹ as well as associative memory consolidation³². The typical delay for hippocampal consolidation processes starts at approximately one hour^{20,25–27}. Therefore, we showed that enhanced self-relevance and recruitment of BSC-related processing in the present experiments improves not only the memory for contextual details of real life-like events, but also the contextual details of seemingly irrelevant events at the time of encoding, which gained importance only later in time. These findings are raising many questions, especially about the relation between self-relevant information and bodily-self processes in time.

To conclude, our current work provides a new evidence for selective and retroactive consolidation of conscious self-experiences that are conceptually related to future events, which

are linked to the processing of multisensory bodily signals. A compelling implication of our findings suggest that it may be critical to temporarily store seemingly irrelevant everyday life episodic autobiographical details, because they may gain future relevance. Future work, including neuroimaging should investigate whether the post-encoding memory consolidation processes that are underlying the results as described in the present experiments and those by previous authors rely on similar or distinct mechanisms.

Methods

Participants

The sample of experiment 1 consisted of 15 right-handed participants ($M = 26.1$, $SEM = 0.9$, 10 female). The study sample of experiment 2 consisted of 16 right-handed participants ($M = 25.3$, $SEM = 1.6$, 10 female). The sample size was based on the sample size from our previous study ¹⁵. Informed consents were obtained from all our participants. The study was approved by the local ethical committee and the two experiments were conducted in conformity with the Declaration of Helsinki.

Reality Substitution technology (RealISM)

Similar to our previous study ¹⁵, we created realistic outside scenes, from which participants could see their own hands, trunk and legs from 1PP. Participants felt immersed into the pre-recorded scenes and seeing themselves present there. The VR technology included spherical capture and recording system for 1PP simulations of real-life environments. 16 cameras and microphones covered the whole sphere of perception around a viewpoint (over 360° horizontally and vertically, stereoscopic vision, binaural panoramic audio). RealISM software combined all data into a high-resolution panoramic audiovisual computer format (equivalent to more than 4 stereoscopic full HD movies). A head-mounted display (HMD, 640 x 800 resolution, 110° diagonal field of view; Oculus Rift Development kit; Oculus VR) was used to immerse participants into the pre-recorded outside scenes. Stereoscopic depths cameras were attached on the HMD to capture participants' bodies (i.e. cameras were on/off) from the 1PP.

Experiment 1

Encoding Session

Participants were immersed in 2 different outside scenes. In the beginning of the experiment, a ball appeared in each of the 2 outside scenes and started to freely move around for 30 seconds.

Participants were asked to visually follow a movement of the ball. This attention task was created in order to assure that participants fully explored both of the 360° pre-recorded scenes. Moreover, participants were asked to follow the trajectory of the ball by physically pointing at the moving ball with their finger.

Retrieval Session

One hour after the encoding session, participants re-visited the same outside scenes they explored during the encoding. There were 3 blocks of 40 trials, each trial lasting 10 seconds. Within the 3 blocks of 40 trials, 10 trials were presented as exactly the same as during the original encoding session (i.e. including the same previously presented everyday-life 10 objects). 30 trials were modified and presented with either 1, 2 or 3 new objects replaced by the old ones. The blocks and individual trials were presented in a randomized order. Participants were free to re-explore each outside scene for 10 seconds, after which they were asked two questions. The instructions were displayed on a black background of the HDM display. First, participants were asked whether each scene looked exactly the same as when they first saw it. Participants were holding a wireless computer mouse, by which they provided the answers (i.e. yes/no). Second, participants were asked how confident they were about their answer. The scale, which appeared in their HDM display was from 0 to 6 and by pressing the computer mouse, participants selected their answers.

Experiment 2

Encoding Session

In experiment 2, participants were asked to explore 2 empty inside rooms and 2 empty outside scenes for 15 seconds. After the 15 seconds, participants were immersed into the same rooms and outdoor scenes again. There was one object at the time appearing in each environment for 10 seconds. Participants were asked to find the object and press a button of a wireless computer mouse if they found it. All participants understood the instructions and successfully found each object in the outside scenes and inside rooms. In total there were 40 objects presented during the pre-body phase (phase 1). After 5 minutes break, participants were immersed into 2 novel empty inside rooms and 2 novel empty outside scenes for 15 seconds. During this body x nobody phase (phase 2), participants were first asked to explore the 4 empty environments. After the 15 seconds, participants were immersed into the same rooms and outdoor scenes again. There was one object at the time appearing in each environment for 10 seconds. Participants were asked to find the object and physically point at it if they found it. All

participants understood the instructions and successfully found each object in the outside scenes and inside rooms. The main manipulation (i.e. the presence or absence of one's physical body) was specific to either 2 inside rooms or 2 outside scenes in phase 2. Crucially, in the body condition, participants could see their physical hand, trunk and legs while physically pointing at the objects in either the rooms or scenes, while in the nobody condition only the scene, without the body was visible. The presentation of the body x nobody condition was counterbalanced between participants. No explicit instructions to memorize the objects of visited rooms were provided. Participants were not informed that their memory for stimuli encountered during the encoding session would be tested during the retrieval session. Before the actual study, participants were seated in a chair, they were asked to put on the HMD and noise-cancelling headphones to avoid external disturbances and familiarized themselves with the VR technology similarly to experiment 1.

Retrieval Session

Participants were informed that they would re-visit the same outside scenes and inside rooms again in 4 blocks of 20 trials, each trial lasting 10 seconds. Within the 4 blocks of 20 trials, 10 trials were presented with exactly the same 10 objects (old) as during the original encoding session and 10 trials with 10 new objects. Participants were free to re-explore each outside scene and inside room for 10 seconds, after which they were asked two questions. The instructions were displayed on a black background of the HDM display. First, participants were asked whether each object was the same as when they first saw it. Participants were holding a wireless computer mouse by which they provided the answers (i.e. yes/no). Second, as in experiment 1, participants were asked how confident they were about their answer. The scale, which appeared in their HDM display was from 0 to 6 and by pressing the computer mouse, participants selected their answers.

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2.4 Study 4

Capturing the spatiotemporal dynamics of task-initiated thoughts with EEG and fMRI

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Abstract

The temporal structure of self-generated cognition is a key attribute to the formation of a meaningful stream of consciousness. Recent fMRI studies suggested that functionally distinct networks are activated *at the same time* during task-initiated self-generated processing, seemingly in contradiction with overwhelming evidence that information processing evolves through a stream of *discrete* conscious units. Here, we analysed both fMRI resting states and EEG microstates to probe the temporal dynamics of self-generated cognition. Participants were asked to mentally retrieve self-relevant past events or to perform serial mental arithmetic operations, thereby shifting from self-related to self-unrelated thoughts. BOLD activity mapping revealed selective enhanced activity in temporal, parietal and occipital areas during the memory compared to the mental arithmetic condition, evincing their role in integrating the re-experienced past events into conscious representations during memory retrieval. Functional connectivity analysis showed that these regions were organized in two major subparts, previously associated to “scene-reconstruction” and “self-experience” subsystems. EEG microstate analysis allowed studying these participant-driven thoughts in the millisecond range by determining the temporal dynamics of brief periods of stable scalp potential fields. This analysis revealed selective modulation of occurrence and duration of specific microstates in the memory and in the mental arithmetic condition, respectively. EEG source analysis revealed similar spatial distributions of the sources of these microstates and the regions identified with fMRI. These findings imply a functional link between BOLD activity changes in regions related to a certain mental activity and the temporal dynamics of mentation, and support growing evidence that specific fMRI networks can be captured with EEG as repeatedly occurring brief

periods of integrated coherent neuronal activity, lasting only fractions of seconds.

1. Introduction

Spontaneous mentation is neither random nor meaningless (Smallwood and Schooler, 2015), however how to precisely capture the wandering mind and attribute it to specific cognitive thoughts, is yet unclear (Fox et al., 2015). One way to better understand the neural mechanism of self-generated cognition is to instruct participants to think of specific experiences during a certain period with eyes closed (Benoit and Schacter, 2015; Stawarczyk and D’Argembeau, 2015). A recent fMRI study by Axelrod and colleagues (Axelrod et al., 2017) employed this technique to distinguish different brain processes that are at work during internal mentation. They showed, as expected, that the Default Mode Network (DMN) dominated during self-generated processing, independent of the type of mental experience (future/past imagery, episodic memory, empathizing). The authors then compared this activation pattern with the brain responses to specific cognitive tasks, i.e. self-referential processing, scene reconstruction and language-related processing, and showed that different parts of the DMN correlated with these task-related networks. These observations thus suggested that different cognitive processes are activated *at the same time* during internal mentation.

Notwithstanding the importance of this finding in the context of the multi-component account of the DMN, the notion of *simultaneity* is relative. It depends on the time scale we are looking at. Already in 1890, William James postulated that the stream of consciousness is not continuous, but parsed in a series of states of mind (James, 1890). He argued that during such states we have only one conscious thought with a unitary content, however complex it may be, which will be distinct from the thought in the previous or following mind state. Since then, an accumulation of theoretical and experimental evidence supports the concept of spontaneous mental activity as being discontinuous and parsed into a series of conscious states, which behave as discrete spatiotemporal patterns of global neuronal activity. Terms such as “pulses of consciousness” (James, 1890), “perceptual frames” (Efron, 1970), “neuronal workspace” (Baars, 1997; Dehaene et al., 1998), “heteroclinic channel” (Rabinovich et al., 2001), or “structure flow on manifolds” (Huys et al., 2014) describe various concepts of parcellation of consciousness into sequential episodes (for reviews see (Deco et al., 2011; Meehan and Bressler, 2012; Michel and Koenig, 2018)). The prevailing hypothesis of all these concepts is that only one global state exists at any moment in time and that conscious mentation emerges by serial appearance of such states (Seth and Baars, 2005). This appears in contradiction to the observations of the study of Axelrod and colleagues (Axelrod et al., 2017), which states that

different cognitive processes are activated at the same time during internal mentation. The reason for this contradiction is that the temporal dynamics of neural networks observed with fMRI are driven by fluctuations on a time scale of tens to hundreds of seconds, due to the sluggish nature of the hemodynamic response function that drives the activity-related BOLD signals (Prete et al., 2017). This is clearly not the time scale in which cognitive mental activities fluctuate. As pointed out repeatedly by Steven Bressler and colleagues (Bressler, 1995; Bressler and Tognoli, 2006), large-scale neuronal networks have to change on a sub-second time scale to adapt to momentary thoughts. Thus, even if dynamic functional connectivity methods are used to analyse fMRI resting state networks, they cannot capture the fastest, most elementary temporal changes of cognitive activities during spontaneous mentation, and are thus not appropriate to understand the neural mechanisms underlying the temporal flow of thoughts in the wandering mind (Kucyi, 2017).

EEG microstate analysis allows to investigate these fast temporal dynamics of large-scale neural networks and to access information about the functional organization of spontaneous mentation in time (Michel and Koenig, 2018; Van De Ville et al., 2010). EEG microstates reflect brief epochs of coherent neuronal activity that persist for around 100 milliseconds (Khanna et al., 2015; Michel and Koenig, 2018). Previous studies demonstrated that the occurrence, duration and sequence of EEG microstates determine the quality of spontaneous mentation, and as such could represent the basic building blocks of conscious mental processes (Lehmann et al., 1998). EEG microstates thus qualify as the electrophysiological manifestation of the segmentation of ongoing mental activity into short-lasting brain states (Baars, 2002; Changeux and Michel, 2004; Michel and Koenig, 2018). Only a few studies have tried to relate EEG microstates to specific cognitive processes (Lehmann et al., 1998; Milz et al., 2016; Seitzman et al., 2016) and none of these studies compared the EEG microstates directly to the underlying brain networks observed with fMRI during the same processes.

The overall goal of this study was to capture the occurrence of spontaneous thoughts within specific, externally-controlled cognitive domains, using ultra-high field 7T fMRI and high-density 64-channel EEG recordings to obtain both hemodynamic and electrophysiological signatures with high functional sensitivity. Fifteen healthy participants were recorded during spontaneous mentation (hereafter termed “rest condition”) and while focusing their thoughts repeatedly for periods of 20sec with eyes closed on either episodic, self-related memories associated with a briefly presented image (“memory condition”), or arithmetic calculations (“math condition”). Consistent with cognitive tasks that require working memory and direct the attention outside of the self (Corbetta and Shulman, 2002), we chose the math condition as a

control condition in order to selectively de-activate regions that become active in autobiographic episodic memory retrieval (Foster et al., 2012, 2015).

To probe functional changes specific to the distinct cognitive domains, we compared the spatial distribution of local BOLD activity changes, as well as their organization in large-scale networks, across conditions. We then examined the fast temporal organization of the brain's large-scale network dynamics, using the EEG microstate approach. Specifically, we focused on the most basic characteristics of the EEG microstate temporal dynamics: their duration, their frequency of occurrence and their transition probabilities. Finally, we estimated the brain networks generating the EEG microstates and compared them to the fMRI networks.

2. Methods

2.1. Participants and Experimental Paradigm

We included 15 healthy participants (30.5 ± 5.5 years, 5 male/10 female) in this study. The work was approved by the institutional review board of the local ethics committee, and all participants provided written informed consent prior to the experiment.

Each participant underwent three sessions: i. an interview session, ii. an EEG recording session, and iii. an fMRI session. During the interview, all participants performed a classical autobiographical memory questionnaire (ABMQ) (Rubin et al., 2003) in order to select vividly remembered images, which were then used for the EEG and for the fMRI sessions, which included three distinct conditions each (*Figure 1*): eyes-closed rest (6min), mentally retrieving personal past episodes (10min), and mental arithmetic operations (10min). The memory and math conditions comprised twenty 30-s trials each. On each trial, a personal image (e.g., photo of a participant with a birthday cake) or a calculation (e.g., $447-7=$) was presented for 5sec, followed by a 20sec period of closed-eyes during which the participants retrieved the past event or continued to serially subtract/add the given number. After this period, there was a question: "*How much did you relive the original event?*" for the memory task and "*How much attention did you pay to the calculation?*" for the mental arithmetic task. The time allowed to read and respond to the question was 5sec. Participants answered by a button press (1="not at all", to 4="fully"). The ratings confirmed active involvement of our participants with high confidence ratings that were comparable between the EEG ($M=3.2$, $SEM=0.12$) and the fMRI ($M=3.1$, $SEM=0.11$) memory session as well as the EEG ($M=3.5$, $SEM=0.12$) and the fMRI ($M=3.41$, $SEM=0.11$) math session.

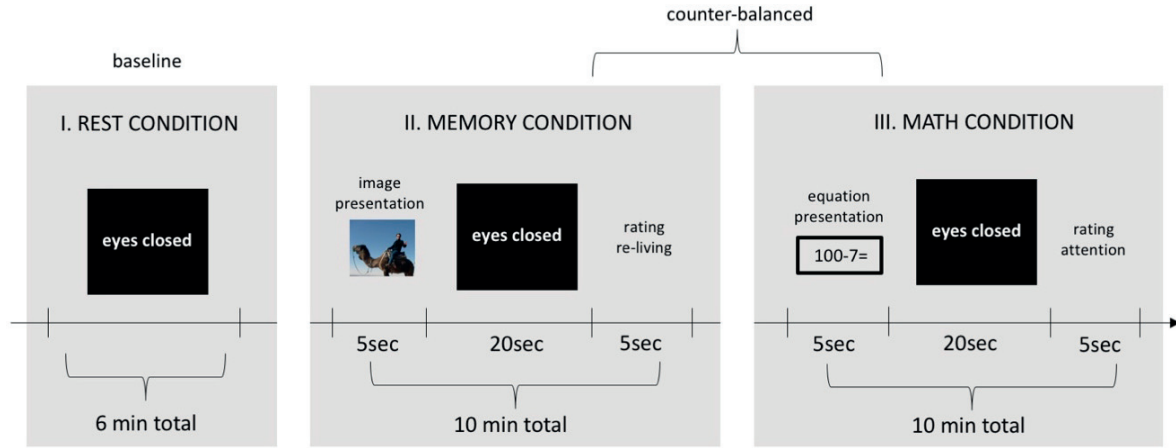


Fig. 1. Experimental paradigm.

Each experimental session started with a 6 min eyes-closed rest condition followed by two counter-balanced experimental conditions. In the memory conditions, participants saw a personal image for 5sec, after which they closed their eyes and had to retrieve the event. After each trial, participants were prompted by a brief flash of light to open their eyes, and answered a control question with a button press: “How much did you relive the original event?” (scale 1= “not at all” to 4= “fully”). Before the scanning, all participants performed a classical autobiographical memory questionnaire (ABMQ) (Rubin et al., 2003) in order to select the 20 most vividly remembered images that were then shown during the task. In the math condition, participants saw a formula presented for 5 sec on the screen. They then closed their eyes and were asked to continually subtract the number from the preceding result for 20 sec. After each trial, participants answered to the question “How much attention did you pay to the calculation?” by button press (scale 1= “not at all” to 4= “fully”).

2.2. fMRI Acquisition and Analysis

2.2.1. fMRI Acquisition

The fMRI sessions were conducted on an actively shielded Magnetom 7T head scanner (Siemens, Erlangen, Germany), equipped with AC84 head gradients (80mT/m max. gradient strength, 333 T/m/s max. slew-rate) and an 8-channel transmit/receive head loop array (Rapid Biomedical, Rimpar, Germany). During each paradigm, whole-brain functional data were acquired using a simultaneous multi-slice (SMS) 2D GE-EPI sequence, with TR/TE = 1000/22ms, $\alpha = 54^\circ$, 110×110 matrix size with 2.0 mm isotropic spatial resolution, 75 sagittal slices with $3 \times$ SMS acceleration and $1/3$ field-of-view (FOV) CAIPI shift (Setsompop et al., 2012), $2 \times$ in-plane GRAPPA acceleration (anterior-posterior direction) and $7/8$ partial Fourier undersampling. This protocol was designed to simultaneously provide fairly high temporal resolution (1 volume/s) and spatial resolution (2-mm voxel width), with whole-brain coverage. For each subject, an additional 5-volume scan was also performed with reversed phase encoding direction (posterior-anterior), for subsequent correction of susceptibility-induced EPI distortions. To aid spatial co-registration, T_1 -weighted anatomical data were acquired with a 3D MP2RAGE sequence (Marques et al., 2010) with TR/TI₁/TI₂/TE = 5500/750/2350/1.87 ms and 1.0 mm isotropic spatial resolution.

2.2.2. fMRI Pre-processing

The fMRI data were processed using the FMRIB Software Library (FSL v5.0, Oxford, UK) combined

with Matlab routines developed in-house (Mathworks, Natick MA, USA). Data pre-processing included motion correction (MCFLIRT tool, 6 degrees of freedom) (Jenkinson et al., 2002), slice-timing adjustment (set to the middle of each TR, via linear interpolation), brain segmentation (BET tool) (Smith, 2002), Gaussian spatial smoothing (FWHM = 4mm) and temporal de-trending (100sec cut-off). To reduce contributions from head motion, a set of 24 confound regressors derived from the motion parameter time courses were regressed out of the fMRI data by general linear model analysis. Each dataset was co-registered to the standard MNI space as follows: first, for each subject, the fMRI data were B₀-unwarped using FSL-TOPUP (Andersson et al., 2003) and brought to the subject's anatomical space using FLIRT with boundary-based registration (Greve and Fischl, 2009) (12 degrees of freedom). The co-registration to MNI space was then determined using the anatomical images, again through FLIRT (12 degrees of freedom).

2.2.3. Fractional Amplitude of Low Frequency Fluctuations (fALFF) Analysis

Voxel-wise fALFF values were estimated for the pre-processed fMRI data of each subject and paradigm, in native space, as proposed by Zou et al. (Zou et al., 2008): the time series of each voxel was transformed to the frequency domain and the sum of amplitudes in the 0.01–0.08 Hz interval was divided by the sum of amplitudes of the full frequency band. The individual fALFF maps thus obtained for each paradigm and subject were then brought to MNI space for group analysis. The fALFF maps were compared between the memory and math conditions using paired T-tests across subjects, and statistical significance was determined using topological false-discovery rate (FDR) inference to correct for multiple comparisons (Chumbley et al., 2010) (cluster-forming threshold $T > 2.20$, FDR $\alpha = 5\%$).

2.2.4. Functional Connectivity Analysis

The brain regions (clusters) displaying significant fALFF changes between the memory and math conditions were further considered for connectivity analysis. These regions were warped to each individual run's native space, and the voxels belonging to each region were identified. The functional connectivity between each pair of regions was estimated as the average Pearson correlation value between the full time course of every voxel in the first region with that of every voxel in the second region. The estimations were organized in a connectivity matrix, and also included an estimation for each region paired with itself, serving as a measure of functional homogeneity within the region.

2.3. EEG Acquisition and Analysis

2.3.1. EEG Recording and Pre-processing.

EEG was recorded with a 64-channel BrainAmp EEG system (Brain Products, Munich, Germany) at 5000 Hz. Offline, the EEG was down-sampled to 250Hz and band-pass filtered between 1 Hz and 40 Hz using a noncausal filter (2nd order butterworth Low and High pass, - 12 db/octave roll-off, computed linearly forward and backward, eliminating the phase shift, and with poles calculated each time to the

desired cut-off frequency). Infomax-based Independent Component Analysis (ICA) was applied to remove oculomotor and cardiac artefacts based on the channels with maximal amplitude, the topography, and time course of the ICA component. Bad electrodes were then interpolated using a 3-D spherical spline (Perrin et al., 1989) and the data was re-computed to the common average-reference. For the memory and the math condition, all 20 sec epochs of eyes closed were concatenated. Finally, the data were visually inspected and periods with remaining artefacts were marked and excluded from further analysis.

2.3.2. K-means clustering

The free academic software Cartool was used for the microstate analysis (Brunet et al., 2011). A modified k-means cluster analysis (Pascual-Marqui et al., 1994) was applied to the data of each subject and condition. Only maps at local maxima of the Global Field Power (GFP) entered the cluster analysis, as they represent time points of highest signal-to-noise ratio (Koenig and Brandeis, 2016). Polarity of the maps was ignored in the clustering. Cluster-analysis was applied in two steps: first on the data of each individual subject and condition, and then on the cluster maps derived from each subject within a condition. In order to determine the optimal number of clusters (both within and across subjects), 7 criteria were used to evaluate independently the quality of each clustering. They were then merged together in order to derive a single synthetic meta-criterion (Custo et al., 2017). This improves confidence in the right estimation of the optimal number of clusters, as compared to previous work relying on a single criterion only (i.e. Cross-Validation criterion (Pascual-Marqui et al., 1995) or the Krzanowski-Lai Index (Murray et al., 2008)).

The following 7 criteria were taken from (Charrad et al., 2014; Krzanowski and Lai, 1988; Milligan and M. C.Cooper, 1985; Pascual-Marqui et al., 1995):

1. *Gamma*: An adaptation of Goodman and Kruskal, based on concordant vs. discordant clustered pairs.
2. *Silhouettes*: Evaluation of the consistency of each cluster through its goodness of fit.
3. *Davies and Bouldin*: A function of the sum of the ratio of within-cluster to between-cluster separation.
4. *Point-Biserial*: A point-biserial correlation calculated between the distance matrix and a binary cluster index.
5. *Dunn*: An evaluation of the goodness of separation of all clusters.
6. *Krzanowski-Lai Index*: A ratio of the relative difference of the within-clusters dispersion.
7. *Cross-Validation*: A modified version of the predictive residual variance.

The meta-criterion was defined as the median of all optimal numbers of clusters across all criteria. The meta-criterion calculation is implemented in the free academic software Cartool (<https://sites.google.com/site/cartoolcommunity/>).

2.3.3. Back-fitting

The group cluster maps of a given condition were fitted back to the original EEG of each subject, including all data points (not only GFP peaks), except for periods that were marked as artefacts. Back-fitting means that the spatial correlation between the cluster maps and each individual data point was calculated and the data point was labelled with the cluster map that showed the highest correlation (winner takes all, see e.g. (Britz et al., 2010; Van De Ville et al., 2010)). Note that the polarity of the maps was ignored in this back-fitting procedure. Data points where none of the cluster maps reached a correlation higher than 50% were labelled as “non-assigned”. Once the whole recording was labelled, a temporal smoothing was applied by ignoring segments where a given cluster map was present for less than 4 time points (32ms) and the time points were split and assigned to the preceding and following cluster map. Two temporal parameters were then quantified for each recording of each subject: the mean duration a given cluster map (microstate) was present without interruption, and the number of times per second a given microstate appeared, independent of the duration – termed “occurrence” (Michel and Koenig, 2018). In addition, we analysed the syntax of EEG microstates by computing the probabilities from a single n^{th} -previous state to the current one for each subject and transition pair and normalized it by all between-class transitions (Lehmann et al., 2005; Tomescu et al., 2018).

2.3.4. EEG source localization

In order to estimate the sources contributing to each of the microstates, we calculated a distributed linear inverse solution (LAURA) (Grave De Peralta Menendez et al., 2004). The lead field for the inverse solution was calculated for 64 electrode positions and the average brain of the Montreal Neurological Institute, in a grey matter-constrained head model using the LSMAC head model with 5000 distributed solution points (Brunet et al., 2011). A standardization across time was applied for each solution point in order to eliminate activation biases (*SI Appendix*, SMethod). The estimated current densities of each subject were then averaged across all time points that were attributed to a given microstate in each condition.

2.3.5. Statistical analysis

The cluster maps derived for each of the three conditions (rest, memory and math) were ordered according to their highest spatial correlation across conditions, and labelled according to the canonical microstate maps described in the literature (Michel and Koenig, 2018). In order to evaluate whether the microstate maps with the same labels were generated by similar networks,

we compared the estimated sources of each cluster map between the three conditions. For that, paired t-tests were calculated for each solution point across subjects and Bonferroni-corrected for multiple testing.

To investigate differences in the temporal dynamics (duration, occurrence) of the microstates between conditions we performed repeated measure ANOVAs with the factors “condition” (rest, math, memory) for each microstate class. We applied a threshold of $p < .0001$ to correct for multiple testing and performed post-hoc comparisons only if this threshold was reached.

3. Results

3.1. Instructed thoughts modulate fMRI networks.

To identify changes in brain activity across different brain regions during the two task-initiated, self-generated processing conditions (math and memory), fALFF values were mapped (Zou et al., 2008), serving as a model-free measure of local BOLD activity (Biswal, 2012). Having obtained a fALFF estimate for each brain voxel of each fMRI run and participant, these values were then compared between conditions on the group level. Condition-specific fALFF changes were found for several cortical and subcortical brain regions. The regions with significantly higher brain activity during the memory compared to the math condition (Fig. 2a) included areas in the parietal, the medial temporal, the prefrontal and occipital lobes. We found dominant activity in the lateral part of the parietal lobe: bilaterally the supramarginal gyrus (lSMG, BA40) and the right angular gyrus (rAG, BA39) of the inferior parietal lobe (IPL). Activity was also found in the medial part of the parietal lobe: the left precuneus (lPCu, BA7), the dorsal part and the ventral part of the posterior cingulate cortex/retrosplenial cortex (dPCC, BA31; vPCC/RSc, BA23). In the temporal lobe we found bilaterally-increased activity in the parahippocampal gyri (lPHG, BA28,35,36) and the right inferior temporal gyrus (rITG, BA21). Significant activity was also found in the right inferior frontal gyrus (rIFG, BA45), and bilaterally in the lateral occipital gyri (lLOCG, BA19). When comparing the fALFF estimates in these brain regions to the non-instructed rest condition (considered as baseline) we found that some of the memory-math differences were due to a stronger increase in BOLD activity during the memory compared to math condition (areas included lPHG and dPCC), while other changes were due to increased BOLD activity during the memory and decreased BOLD activity during the math conditions. Areas de-activated during math compared to rest included rAG, lSMG, lLOCG, lPCu and vPCC/RSc. (Fig. 2b). Conversely, we also identified a set of brain areas significantly more active during the math compared to the memory condition: in the frontal lobe, significantly higher activity was found in the ventral and dorsal anterior cingulate cortex and bilaterally in the dorsolateral prefrontal cortex. Areas in the temporal lobe included bilaterally the superior temporal gyrus and the left middle temporal gyrus. In the parietal cortex, significantly higher activity was found in the right intraparietal sulcus and the pre/post central gyrus as well as the dorsal posterior cingulate cortex. In the occipital cortex the occipital gyrus was activated bilaterally. In contrast to the above observation of areas de-activated during math (compared to the rest

condition), none of the areas with significantly higher activity in the math condition were actually deactivated during the memory condition (*SI Appendix*, Figs. S2a and S2b).

To determine condition-specific networks, we further analysed, in terms of their functional connectivity, the brain regions that demonstrated significant BOLD activity changes between the memory and math conditions, as identified by the fALFF analysis. These connectivity values were organized in matrices, and the regions were re-ordered according to their correlation profiles. The connectivity analysis revealed two distinct networks within the regions that displayed stronger activity during the memory condition (Figs. 2c and 2d). Network I. included the vPCC/RSc, lPHG, lROCG, rITG and lPCu, while network II. comprised the rIFG, rAG, lSMG, and dPCC. Compared to the non-instructed rest condition, both networks displayed strong increases in connectivity amidst their respective regions, while remaining uncorrelated to each other and to the areas identified in the math condition.

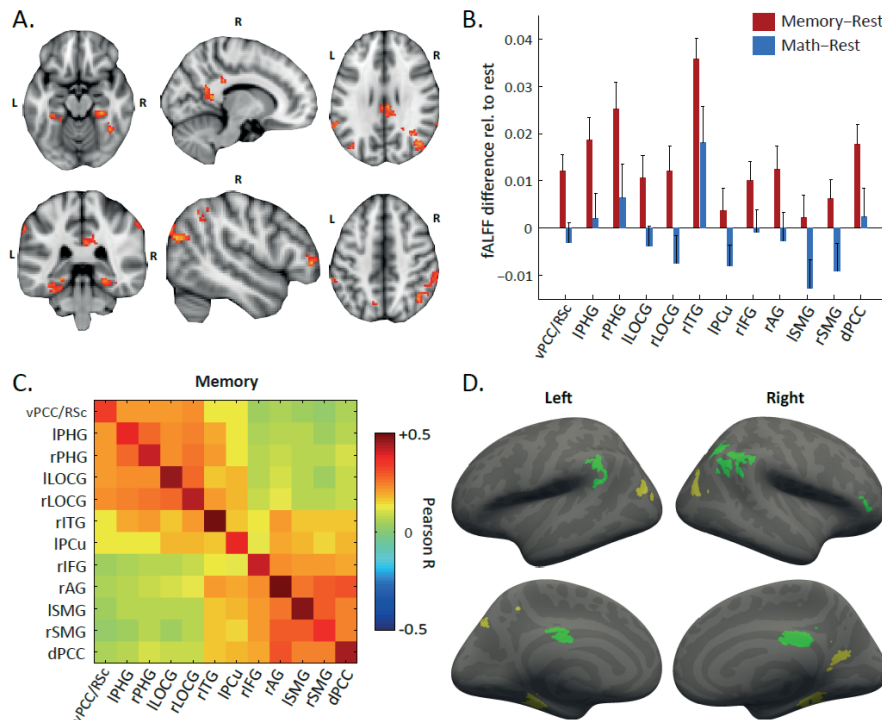


Fig. 2. Memory-specific changes in fMRI activity and fMRI functional connectivity memory sub-networks. **A. fMRI fALFF analysis.** T-test of fALFF for memory > math condition revealed stronger activity in lrSMG, rAG, lrLOCG, lPCu, dPCC, vPCC/RSc, lrPHG, rITG, rIFG. T-score threshold: $T > 2.20$; FDR-corrected for multiple comparisons (5%). **B. Areas of stronger activity in the memory, compared to math condition.** Some of the memory-math differences were due to a stronger increase in BOLD activity during the memory than the math condition relative to rest, while other changes were due to increased BOLD activity during the memory and decreased BOLD activity during the math conditions relative to rest. **C. Connectivity analysis.** Network I. included the vPCC/RSc, lPHG, lROCG, rITG and lPCu, which we called “scene-reconstruction subsystem”. Network II. comprised the rIFG, rAG, lSMG, and dPCC, called “self-experience subsystem”. **D. Sub-networks of the connectivity analysis.** Regions were also projected onto a surface template for better visualization.

3.2. Instructed thoughts modulated the temporal dynamics of specific EEG microstates.

A k-means cluster analysis was first applied to each individual subject and then across subjects within each condition. While the optimal number of clusters varied between subjects, the meta-criterion determined 6 clusters as the optimal number in the clustering across subjects for each condition. The topographies of these six maps were strikingly similar between the three conditions and resembled those previously described in the literature (Michel and Koenig, 2018). We ordered the microstate maps according to their highest spatial correlation across conditions (i.e. math, memory, rest) and labelled them from A-F states (Custo et al., 2017; Michel and Koenig, 2018) (Fig. 3a). Statistical comparison of the underlying brain sources that generated these microstates indicated similar networks between the corresponding maps in the three conditions (*SI Appendix*, Table S1). We then fitted the maps back to the original EEG of each participant and labelled each time point with the microstate that had highest spatial correlation (Fig. 3b). This procedure allowed us to determine the mean duration of each microstate in the three conditions, and how often the microstates occurred independent of their duration.

ANOVA analyses for each microstate revealed that two states (i.e. microstates C and D) significantly differed in their duration and occurrence depending on the condition (Fig. 3c) and one state (i.e. microstate B) significantly differed in its occurrence (Fig. 3d). Microstate B was specific to the memory condition as it significantly increased in occurrence compared to the math as well as to the rest conditions (both $p < 0.0001$). Microstate C significantly decreased in duration and occurrence in the math condition as compared to both, the memory and the rest conditions (both $p < 0.001$). Finally, microstate D was specific to the math condition as it significantly increased in occurrence and duration compared to the memory ($p < 0.001$) and the rest ($p < 0.0001$) conditions.

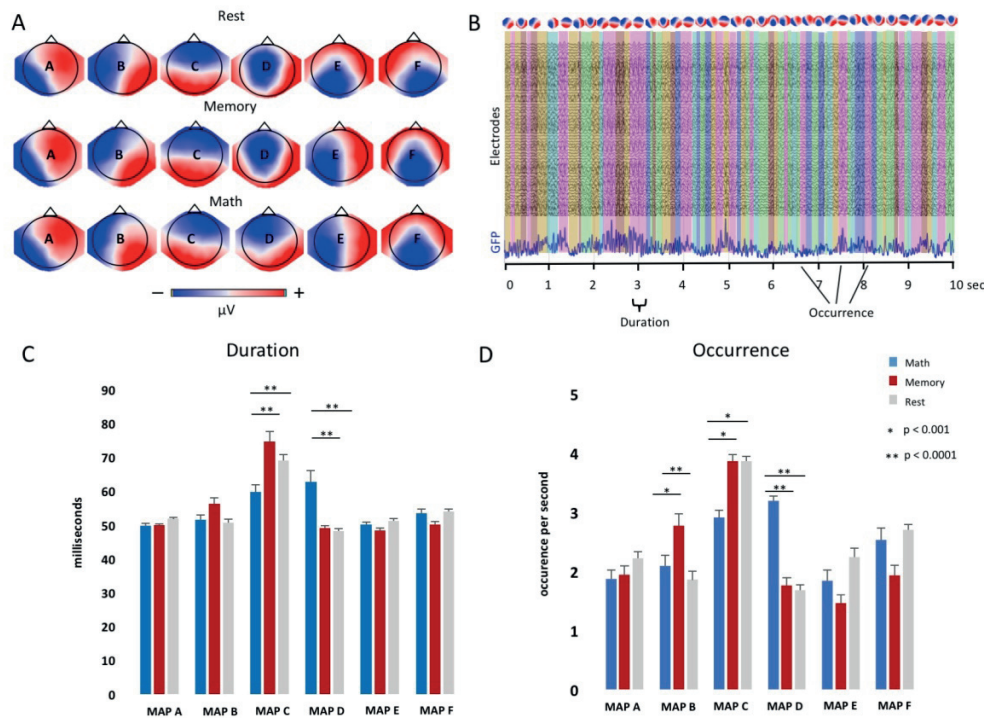


Fig. 3. Temporal dynamics of EEG microstates.

A. The six microstates identified by k-means cluster analysis across subjects in the three conditions (rest, memory and math). **B.** A representative period of 10-sec EEG with eyes closed after picture presentation is shown (traces of 64 electrodes and Global Field Power (GFP) trace). Back-fitting the 6 microstate maps derived from the cluster analysis shows the chunking of the EEG into segments of various durations covered by one of the microstate maps (indicated by different colors). **C.** Mean and standard error of the duration of each of the microstates in each condition. Post-hoc tests were performed when the ANOVA revealed significant condition differences at $p < 0.0001$. This was the case for microstate map C and map D: Microstate C was significantly shorter and microstate D significantly longer in the math condition compared to memory and rest. **D.** Occurrence of the six microstates in the three conditions (number of microstates per second). Significant ANOVAs were found for microstates B, C, and D. As for the duration, microstate C occurred less and microstate D more often in the math condition compared to rest and memory. Concerning microstate B, an increased occurrence was found for memory compared to math and rest.

3.3. Sources of EEG microstates.

To estimate networks underlying each microstate we inverted the original data of each subject into source space using a distributed linear inverse solution (Grave De Peralta Menendez et al., 2004), as described in the Methods. We then averaged the estimated activity across all time points that were labelled with the same microstate maps for each subject and each condition. The brain regions underlying the six microstate maps confirmed and extended previous efforts (Custo et al., 2017) in source localization of microstates (Fig. 4 and Supplementary Figures 3-5). Specifically, microstate A showed left-lateralized activity in the superior temporal gyrus (STG), the medial prefrontal cortex (MPFC) and the OCG. Microstate B showed main activity in OCG and in the medial part of the parietal cortex in the PCu/RSc. The sources of microstate C were located bilaterally in the lateral part of the parietal cortex including both the SMG and AG. The sources of microstate D showed main activity bilaterally in the IFG, dACC, and superior parietal lobule (SPL)/intraparietal sulcus (IPS). Strongest

activity for microstate E was found in the right MPFC. Finally, microstate F showed bilateral activity in the MPFC.

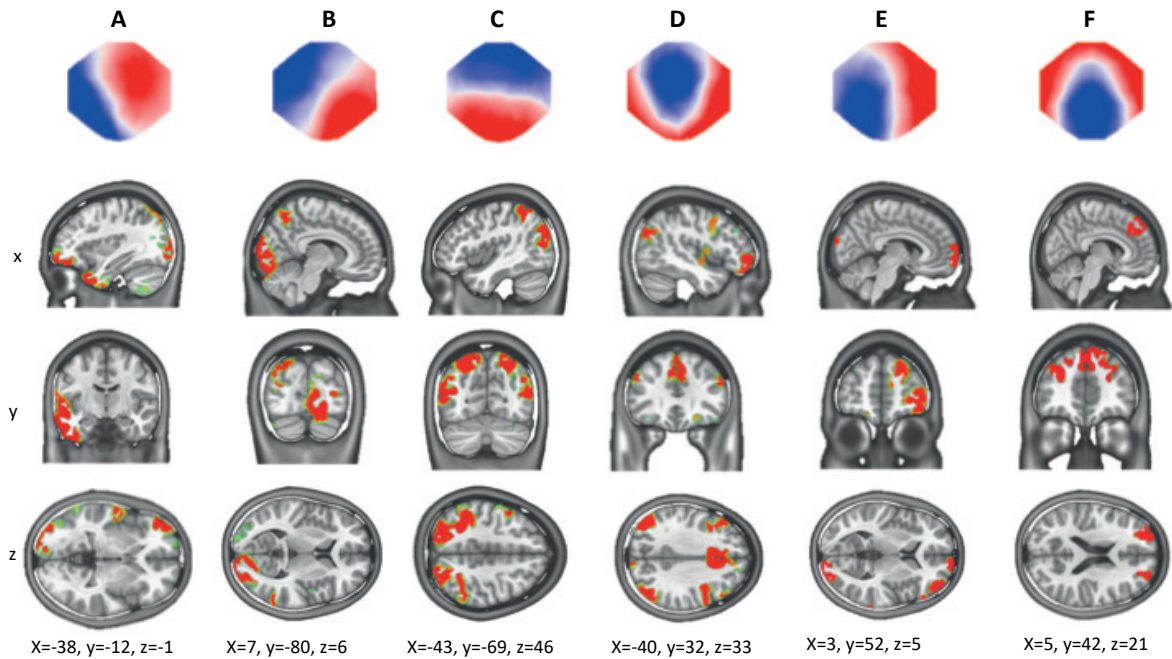


Fig. 4. Source localization of EEG microstates. The EEG of each participant and condition were subjected to a distributed linear inverse solution and standardized across time. The source maps of all time points that were labelled with the same microstate map were then averaged within participants. The mean sources across subjects in the memory condition are illustrated here (for individual source maps per condition see *SI Appendix*, S Figs. 3-5). Areas with activity above 95 percentiles are shown. Notice the strong activity of the superior parietal lobe for microstate C (strong presence in memory and rest) and the frontoparietal activity for microstate D (strong presence in math).

3.4. Transition between memory-related subnetworks.

To determine whether the brain alternates between the two dominating microstates in the memory condition (microstates B and C), we calculated the transition probabilities (normalized by the occurrence) between microstate B and C and compared them to all other possible transitions. We found that specifically and only in the memory condition, the transition from microstate C to microstate B was significantly more frequent than the transition from any other state and that microstate B transitioned significantly more often to microstate C than to any other state (Fig. 5). Likewise, microstate C was significantly more often followed by microstate B than microstates A, D or E, but not F.

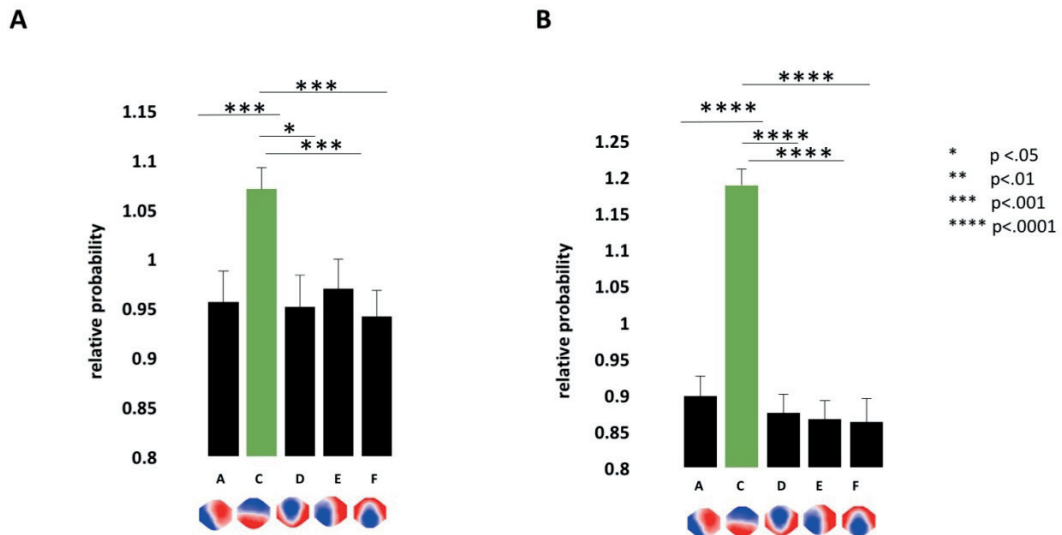


Fig. 5. Markov chain transition probabilities. We calculated the transition probabilities from each microstate to any other using Markov chains. The observed probabilities were divided by the expected probabilities to account for the variability in occurrence of the states. In the memory condition, we found that microstate B was significantly more often preceded (**A**) and followed (**B**) by microstate C than any of the other microstates. This transition behavior was not found during rest or when participants performed mental arithmetic operations.

4. Discussion

By using fMRI and EEG in a paradigm where participants were instructed to focus their thoughts on specific tasks, we here provide direct evidence of capturing the temporal occurrence of specific large-scale brain networks that are involved in self-related and self-unrelated thoughts. In line with previous task-related studies (Andrews-Hanna, 2012; Andrews-Hanna et al., 2014; Axelrod et al., 2017), the fMRI data revealed that thinking about self-experienced past events boosted a brain network known to be related to autobiographic episodic memory, while performing mental arithmetic enhanced a network known to be involved in attention and cognitive control. Intriguingly, the EEG analysis showed that the different conditions produced modulations in the occurrence and duration of brief, sub-second episodes of stable configuration of the brain electric field (the EEG microstates). Source localization of these episodes revealed networks that spatially coincided to those observed with fMRI.

Crucially, in this study, we sought to build upon previous fMRI work that applied experimental designs with faster alternating conditions (each lasting for less than 30s) (Axelrod et al., 2017), to explore a design where all trials of each condition are grouped in an individual run lasting for several minutes. This allowed not only the study of changes in BOLD activity for each brain region (through fALFF analysis), but also the study of the interactions between those regions across time (through functional connectivity analysis) throughout the same condition – thereby shedding new light on the question of whether different functional regions that become active

at the same time effectively share similar BOLD activity.

The fALLF analysis confirmed and extended previous studies by revealing condition-specific BOLD changes in several cortical and subcortical brain regions. The regions with significantly higher brain activity during the memory, compared to the math condition, included the core brain areas of the episodic memory retrieval network (Schacter et al., 2012; Spreng and Grady, 2009; Svoboda et al., 2006) in the parietal, the medial temporal, the prefrontal and occipital lobes. Conversely, we also identified a set of brain areas more active during the math, compared to the memory condition, that have been previously associated to mental arithmetic tasks and frontoparietal control network (FPCN) in general (Fehr et al., 2007).

The fMRI connectivity results revealed that the regions of increased fALFF were essentially organized in two subsystems with distinct functional and anatomical characteristics – highly correlated within themselves, but poorly correlated between each other. Network I. was strikingly similar to a previously described subsystem which becomes involved during constructions of mental scenes (hereafter termed “scene-reconstruction subsystem”), while network II. closely matched a previously defined subsystem which becomes active when participants engage in self-relevant cognitive processes and reflect on their current mental states (hereafter termed “self-experience subsystem”) (Andrews-Hanna et al., 2014, 2010; Axelrod et al., 2017).

Beyond the slower timescale of fMRI measures, the EEG microstate analysis revealed new insights into the temporal dynamics of these networks in the sub-second range. We found that specific EEG microstates, representing brief periods of coherent network activity, were selectively increased in duration and occurrence by the instructed thoughts. The brain regions generating these microstates overlapped with the specific fMRI networks. The network underlying microstate C, which occurred more often and lasted longer in the memory compared to the math condition, largely overlapped with the lateral parietal areas of the “self-experience” memory retrieval subnetwork that we identified in the fMRI analyses. On the other hand, the brain areas underlying microstate B, which selectively increased in occurrence during the memory condition, overlapped with the medial parietal and occipital areas of the “scene-reconstruction” subnetwork that we detected in the fMRI analyses. Finally, brain areas underlying microstate D, which selectively increased in duration and occurrence in the math condition, included areas generally attributed to the frontoparietal control network (FPCN) (Ptak et al., 2017).

Moreover, during memory retrieval, we found increased transitions between the microstates that corresponded to the “self-experience” and “scene-reconstruction” subnetworks in the fMRI

data. These results provide direct evidence that the RSNs captured by fMRI are tightly linked to, and possibly originated by, a prolongation and repeated occurrence of states of synchronized activity of specific large-scale neuronal networks, in the sub-second timescale. Most importantly, the EEG microstate analysis provides compelling evidence that these subnetworks are not activated at the same time, as concluded by Axelrod and colleagues (Axelrod et al., 2017), but that they are sequentially and repeatedly activated over time in the sub-second range, supporting the different models of parcellation of cognition into different mind states (Baars, 1997; Deco et al., 2011; Dehaene et al., 1998; Efron, 1970; Huys et al., 2014; James, 1890; Meehan and Bressler, 2012; Michel and Koenig, 2018; Rabinovich et al., 2001). The fMRI connectivity results are in good agreement with this finding, showing a clear functional dissociation between the two memory subnetworks, albeit at the slower timescale of BOLD fluctuations, less directly related to the underlying neuronal activity.

To capture the occurrence of any conscious experience, and to directly investigate the cognitive processes operating during mind-wandering, it is crucial to better control the spontaneous thoughts of participants (Koch, 2018; Kucyi et al., 2016). In line with other recent studies (Andrews-Hanna et al., 2010; Axelrod et al., 2017; Delamillieure et al., 2010), we here initiated periods of spontaneous mentation with brief presentations of external stimuli and instructed participants to close their eyes and internally direct their thoughts to either self-related photographs or self-unrelated arithmetic operations. The main regions that showed increased BOLD activity in the memory condition comprise the IPL and MTL structures. Numerous studies have previously identified these regions as the core of the episodic memory retrieval network (Schacter et al., 2012; Spreng and Grady, 2009; Svoboda et al., 2006). Traditionally, since the discovery of densely amnesic patients, the MTL structures have been regarded as essential for long-term memory formation, allowing us to remember past experiences and to retrieve acquired knowledge (Moscovitch et al., 2016; Steinvorth et al., 2005). In contrast to the MTL structures, extensive evidence from patient lesion and brain stimulation studies suggests that the IPL plays a key role in integrating vivid details of personally experienced events into conscious representations during memory retrieval (Berryhill et al., 2007; Simons et al., 2010). The subjective experience of perceiving a scene, recognizing a face, hearing a sound or reflecting on the experience itself presents a complex interplay between memory, attention and consciousness (Corbetta and Shulman, 2011; Tononi et al., 2016). Tulving (Tulving, 1985) defined the underlying ability to re-experience the subjective sense of self in the past and to mentally project oneself into the future, i.e. the autonoetic consciousness, as the crucial aspect of episodic memory retrieval. Evidence across lesion studies, stimulation and

recording studies consistently point to the posterior regions, including temporal, parietal and occipital areas (“posterior hot zone”) as playing a direct role in specifying the contents of consciousness (Koch, 2018). Our current findings are also in line with a recent study (Bréchet et al., 2018) where we confirmed the contribution of the IPL, especially the AG, to the subjective, first-person perspective re-experience of self-relevant, vivid past episodes.

Brain activity constantly fluctuates in and out of different mental states that are stable for fractions of seconds. Only one epoch or state of conscious content can be considered at a time (Seth and Baars, 2005). It is assumed that the EEG microstates capture these states that last for around 100 milliseconds only (Baars, 2002; Changeux and Michel, 2004). Using high-density whole-brain EEG, we indeed observed modulations of duration, occurrence, and transitions between particular microstates by the instructed thoughts, microstate B and C being increased in the memory condition and microstate D being increased in the math condition. The topographies of these three microstates strongly resemble three of the four canonical microstates previously described in the literature (for reviews see (Khanna et al., 2015; Michel and Koenig, 2018)). Studies on large cohorts showed that microstate C is generally the most dominant state during eyes-closed rest (Koenig et al., 2002; Tomescu et al., 2014). Recently, Seitzman et al. (Seitzman et al., 2016) showed that microstate C decreases in duration and occurrence during a mental arithmetic task, similar to our findings. Decrease of microstate C duration has also been described when subjects are engaged in object or verbal visualization tasks compared to rest (Milz et al., 2016). Based on these and other studies, it is assumed that microstate C reflects activity in the DMN (Custo et al., 2017; Milz et al., 2016; Panda et al., 2016; Seitzman et al., 2016); for a discussion, see (Michel and Koenig, 2018). Indeed, our analysis of the sources underlying this microstate confirms such interpretation. The sources of microstate C were located bilaterally in the lateral part of the parietal lobe and MTG, areas that we attributed in the fMRI results to the “self-experience subsystem”. The observation that microstate C is not significantly boosted by the memory condition compared to rest is not surprising. It confirms the assumption that self-relevant memory retrieval also predominates during spontaneous mind wandering.

Moreover, our investigation revealed that microstate B increased in occurrence during the memory as compared to both rest and math conditions. This state has been previously attributed to the visual network (Britz et al., 2010; Custo et al., 2017, 2014). For example, Milz and colleagues (Milz et al., 2016) showed that microstate B increased when participants were asked to visualize previously presented images. Source localization in our study also indicated strong

activation of the visual cortex together with medial parietal areas. Intriguingly, lesions to the medial parietal cortex cause memory recognition and visuospatial impairments, but no impairments related to self-consciousness (Davidson et al., 2010). We thus interpret the increased occurrence of microstate B as related to the “scene-reconstruction subsystem” found in the fMRI connectivity analysis. An intriguing assumption is therefore that the microstate analysis allows us to disentangle the sub-parts of thoughts related to the conscious experience of an episodic autobiographic memory, i.e. visualization of the scene and visualization of the self in the scene. Indeed, the transition probability analysis revealed a more frequent switching between microstate B and C than between any other state.

Additionally, our results show that while both microstates B and C are less frequently appearing when participants are engaged in math calculations, microstate D strongly increases in duration and occurrence during this condition. Microstate D has previously been attributed to the attention/cognitive control network including frontoparietal areas (Britz et al., 2010; Custo et al., 2017) and our source localization of microstate D confirmed the attribution of this state to the frontoparietal control network (FPCN) (Ptak et al., 2017). Furthermore, the observation of increase of microstate D and decrease of microstate C fits very well to the observation that the FPCN and the DMN are inversely activated when participants are engaged in external-directed and self-directed cognition (Dixon et al., 2018). Therefore, we show that the large-scale network anti-correlation found in the fMRI data is associated with sub-second modulation of the presence of microstates sub-serving these functions.

EEG microstate studies have repeatedly revealed changes of the temporal dynamics of microstates in mental disease, particularly schizophrenia (for reviews see (Khanna et al., 2015; Michel and Koenig, 2018)). The most robust finding, confirmed in a recent meta-analysis (Rieger, 2016), is an increase in duration and occurrence of microstate C and a decrease of microstate D in patients with schizophrenia (Koenig et al., 1999; Lehmann et al., 2005) or at risk to develop schizophrenia (Andreou et al., 2014; Tomescu et al., 2014), a disequilibrium that is normalized when patients are treated with antipsychotic medication (Kikuchi et al., 2007) and with rTMS (Sverak et al., 2018). These findings correspond well to the interpretation that microstate C reflects introspective, self-focused thoughts, while microstate D reflects attention and cognitive control. An increase of microstate C and decrease of microstate D in schizophrenia might index the progressive detachment of mental states from environmental input. While a healthy person constantly and effortlessly balances periods of rest with periods of focused attention when interacting with their surroundings, patients with schizophrenia or

other mental disorders may persist on thinking about a particular unpleasant event that involves themselves and lose control over the natural flow of the wandering mind. Understanding the functional significance of microstates with studies as the one presented here might thus not only be relevant for monitoring the vulnerability of patients at risk for mental disease and the effects of treatment, but also for better understanding the thoughts that these patients are caught in.

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Supplementary Method

EEG source localization normalization: After the inverse solution matrix has been applied to the ongoing EEG at each time point, a standardization of the estimated current density across time was applied to each solution point. As a matter of fact, substantial variability of power is observed across solution points when localizing the sources on ongoing (non-averaged) EEG in individual subjects. These variations are supposed to come from geometrical and mathematical approximations that are done during the inverse matrix calculation. It is thus necessary to find a way to correct for this power variability, in order to correctly estimate the fluctuations of brain activity over time in individual subjects and to compare them between

subjects (*Supplementary Figure*, Fig. S1).

The main idea here is to use the background activity of the norm of the inverse solution over time to estimate a baseline and a scaling factor for each solution point. In order to have a robust estimation, a large enough time sample should be used, preferably the whole recording as it was done in this study. Still, the correction factors can be satisfactorily computed on as little as a thousand time points, as long as no solution point remains in the same stable state more than half of the sampled time.

Here is a step-by-step description of this specialized standardization:

Given a 3D dipole (sp_x, sp_y, sp_z) at a given solution point sp , we define sp_χ as the squared value of its norm (Equ. 1). It therefore follows a Chi-square distribution of degree 3 for the noisy part of the data. The Chi-square variable sp_χ can be transformed into a normally distributed variable sp_N (Equ. 2) (12). Having now a normal distribution, it can be standardized into sp_Z by using the regular z-transform (Equ. 3). However, the values of μ and σ used for the z-transform have to be calculated only on the noisy part of the data - the background activity from the Chi-square i.e. the lowest values of the distribution. Hence μ is estimated from the left-most Mode of the sp_N distribution (Equ. 4). For the same reason, σ is estimated from the Median of Absolute Deviation (MAD), centred on the previously estimated μ , and computed only with the values below μ (Equ. 5). Implementation-wise, these estimators are computed multiple times on random sub-samplings of the data, and the two respective medians of all these estimators are finally taken.

Finally, because we started with positive data (the norm of a dipole), we also wish to end up with positive data, as to avoid any confusion due to having signed results. We define sp_{Z+} as sp_Z shifted by 3 standard deviations to the right, then divided by 3 so that the background mode is finally aligned to 1 (Equ. 6).

$$sp_\chi = sp_x^2 + sp_y^2 + sp_z^2 \quad (\text{Equ. 1})$$

$$sp_N = (sp_\chi/3)^{1/3} \quad (\text{Equ. 2})$$

$$sp_Z = (sp_N - \mu_{sp_N})/\sigma_{sp_N} \quad (\text{Equ. 3})$$

$$\mu_{sp_N} = \widehat{Mode}_{left}(sp_N) \quad (\text{Equ. 4})$$

$$\sigma_{sp_N} = \widehat{MAD}_{left}(sp_N) \quad (\text{Equ. 5})$$

$$sp_{Z+} = \max((sp_Z + 3)/3, 0) \quad (\text{Equ. 6})$$

The result of this standardization procedure is comparable power of the current density across

all solution points, and a normal distribution of the solution points (*Supplementary Figure*, Fig. S1).

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Supplementary Figures

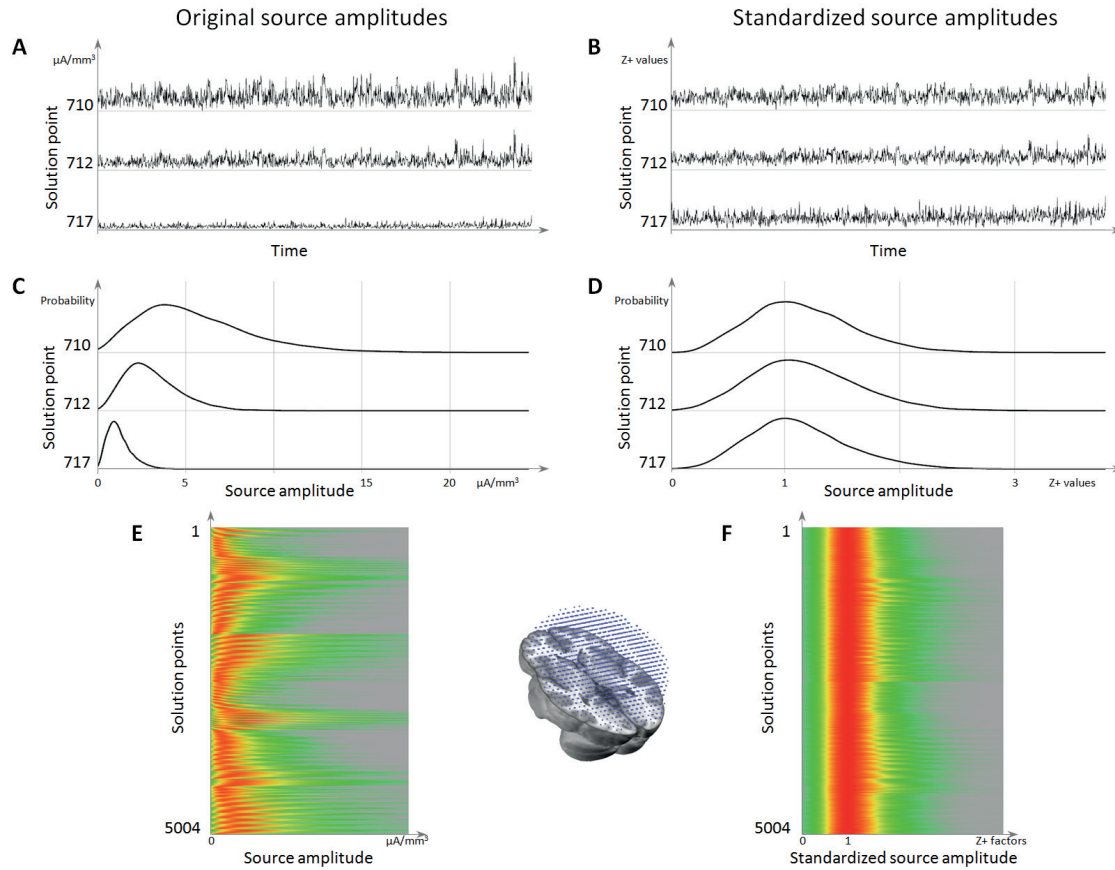


Fig. S1. Source localization standardization. **A.** is the time series (horizontal axis) of 3 solution points (vertical axis), showing the difference in power range between them. **C.** is the histograms of these 3 solution points, showing that the background activity is the left-most mode of the distribution. **E.** is the histograms for all solution points (vertical axis), with the red color coding for the maximum probability. **B.** is the same time series as in **A** but after standardization, showing that the 3 solution points now have the same range. **D.** is the histograms after standardization, showing that all the background activity has been centered to 1. **F.** is all histograms after standardization, showing that all solution points now have a background range from 0 to 1, while retaining their respective highest activities.

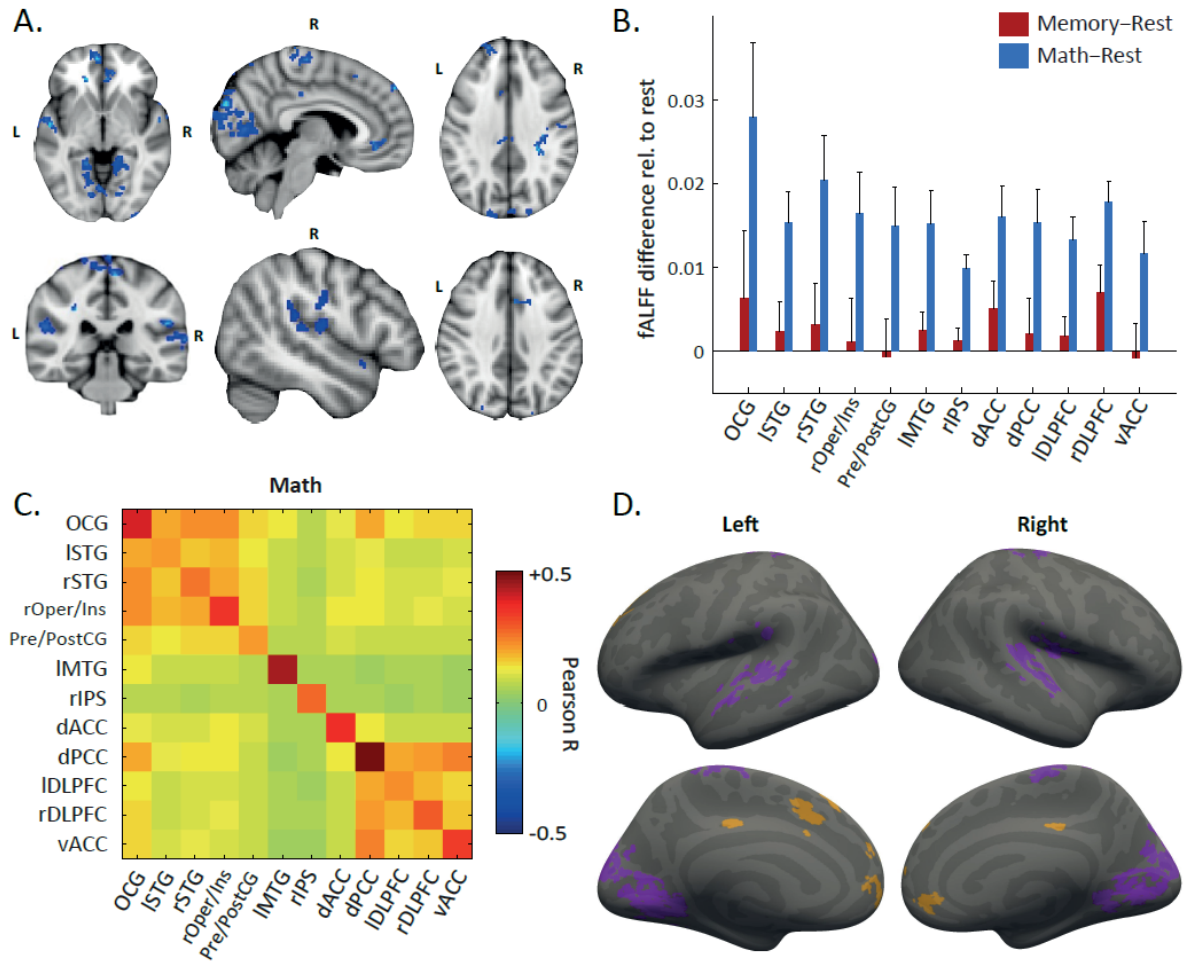


Fig. S2. Math-specific changes in fMRI activity and fMRI functional connectivity networks.

A. fMRI fALFF analysis. T-test of fALFF for math > memory condition revealed stronger activity in a set of brain areas. In the frontal lobe, significantly higher activity was found in the ventral and dorsal anterior cingulate cortex (vACC, BA24; dACC, BA32), and bilaterally in the dorsolateral prefrontal cortex (lrDLPFC, BA46). Areas in the temporal lobe included bilaterally the superior temporal gyrus (lrSTG, BA22), the left middle temporal gyrus (IMTG, BA21), and the right opercular cortex/insula (rOper/Ins, BA45). In the parietal cortex, significantly higher activity was found in the right intraparietal sulcus (rIPS, BA7) and the pre/post central gyrus (Pre/PostCG, BA3,1) and dorsal posterior cingulate cortex (dPCC, BA30). The occipital findings concerned the occipital gyrus bilaterally (OCG, BA19). T-score maths > memory threshold: $T > 2.20$; FDR-corrected for multiple comparisons (5%). **B. Areas of stronger activity in the math, compared to memory condition.** In contrast to the above observation of areas de-activated during math (compared to the rest condition), none of the areas with significantly higher activity in math compared to memory were actually de-activated during the memory condition. **C. Connectivity analysis.** The connectivity analysis revealed two distinct networks within the regions that had displayed stronger activity during the math condition: network III included the OCG, lrSTG, rOper/Ins and Pre/PostCG, while network IV comprised the dACC, dPCC, lrDLPFC and vACC. Beyond their strong intrinsic connections, the two networks were also moderately connected to each other, unlike what was observed for the memory-related networks. The IMTG and rIPS regions displayed no relevant correlations with any of the two networks, or with each other. **D. Sub-networks of the connectivity analysis.** The two identified networks were also projected onto a surface template for better visualization.

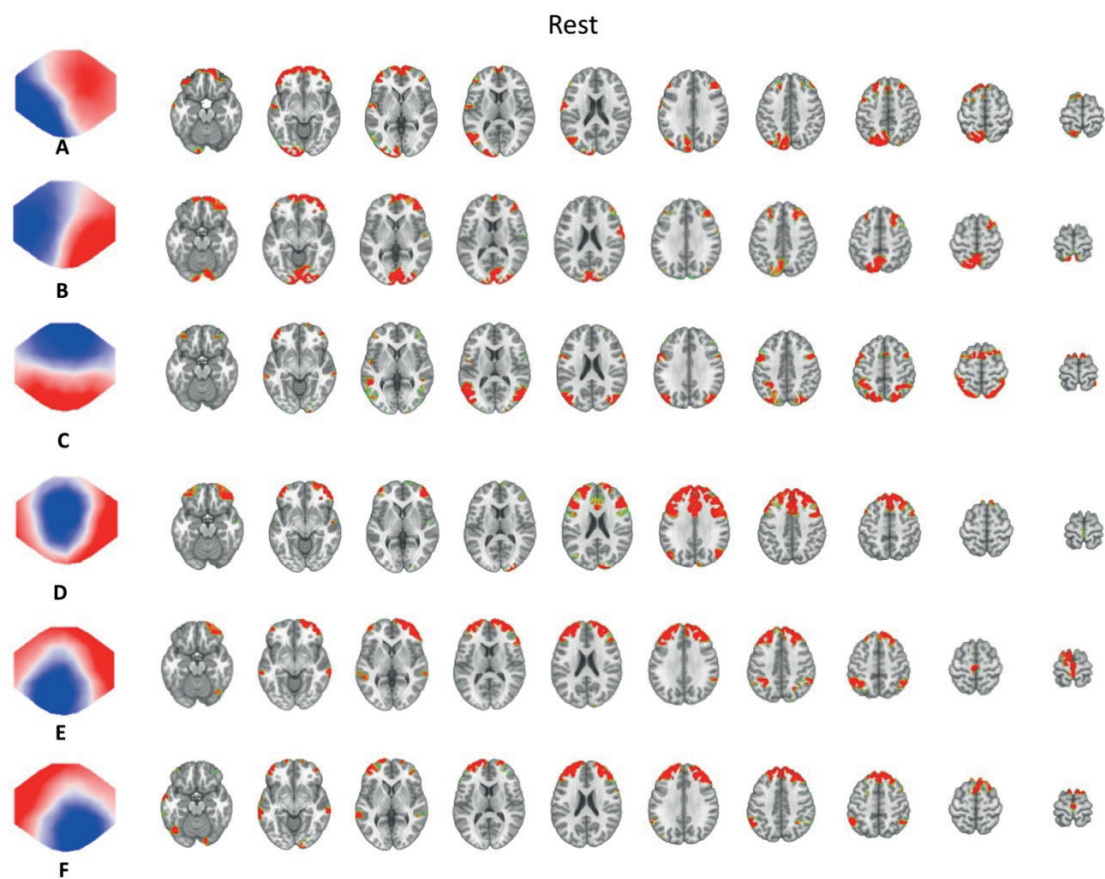


Fig. S3. Source localization of the six microstates during the rest condition. Sources are averaged across all time points that were labelled with the corresponding map and averaged across subjects. Areas with activity above 95 percentiles are shown.

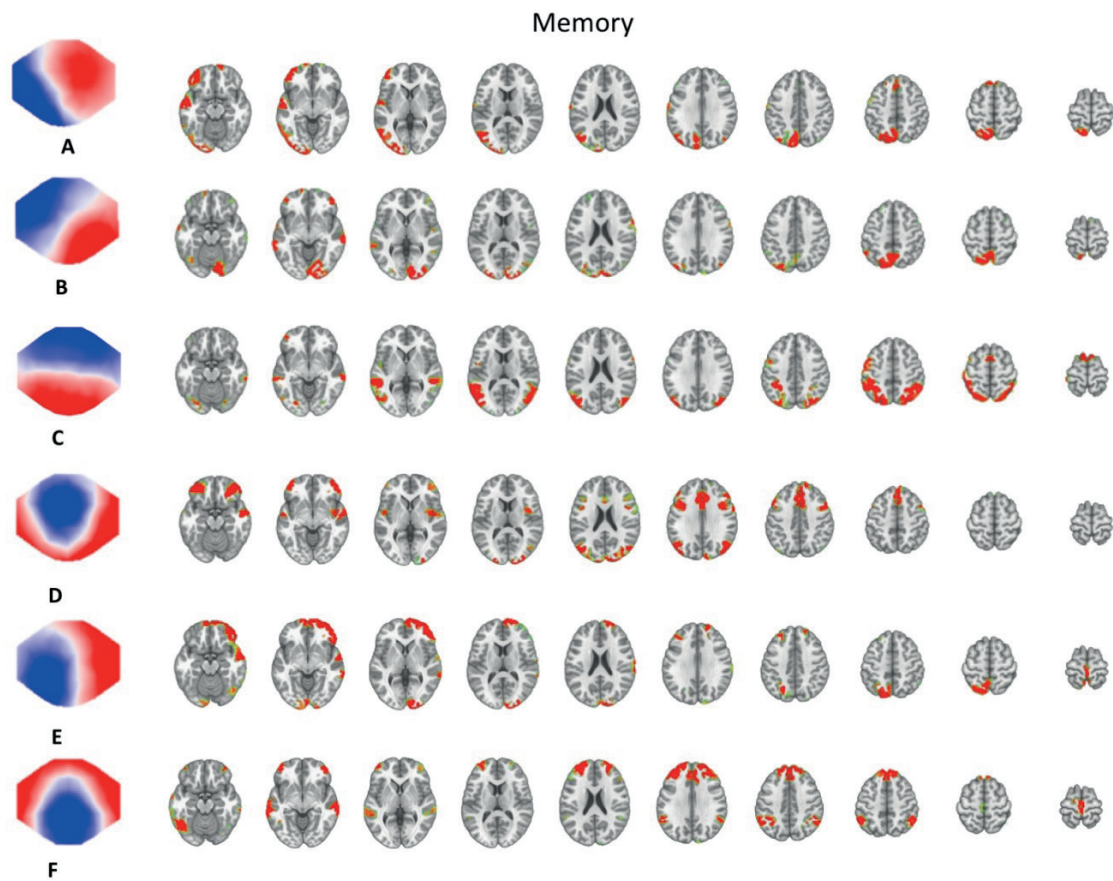


Fig. S4. Source localization of the six microstates during the memory condition. Sources are averaged across all time points that were labelled with the corresponding map and averaged across subjects. Areas with activity above 95 percentiles are shown.

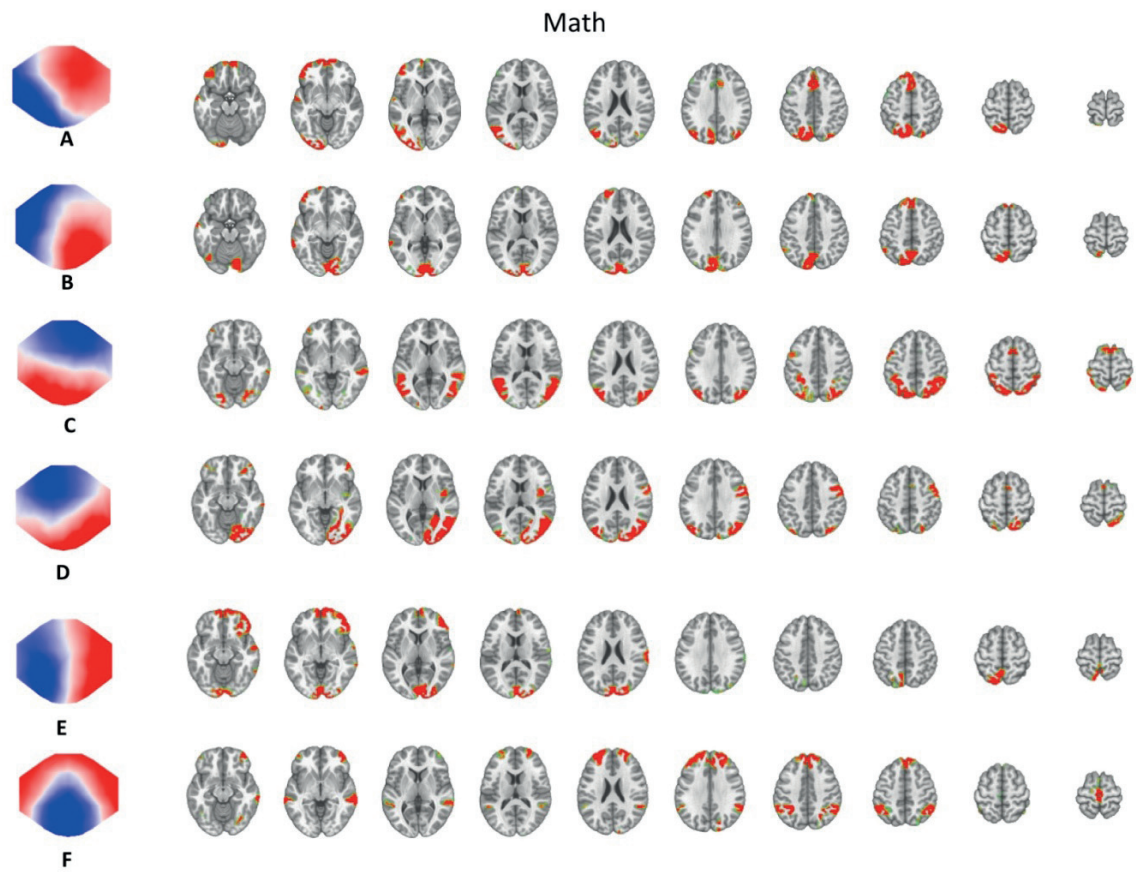


Fig. S5. Source localization of the six microstates during the math condition. Sources are averaged across all time points that were labelled with the corresponding map and averaged across subjects. Areas with activity above 95 percentiles are shown.

		MEMORY					
MATH	Microstate	A	B	C	D	E	F
	A	NS 5	** 12	** 16	** 14	* 11	** 20
	B	** 15	NS 7	** 18	** 17	* 11	** 16
	C	* 10	* 11	NS 5	* 11	* 10	** 16
	D	** 15	NS 7	** 14	NS 9	* 10	** 16
	E	** 14	** 12	** 16	** 14	NS 6	** 24
	F	** 14	NS 9	** 15	* 11	*** 12	NS 7

		MEMORY					
REST	Microstate	A	B	C	D	E	F
	A	NS 5	* 10	* 11	** 12	* 10	** 13
	B	** 13	NS 6	* 11	** 12	NS 6	** 16
	C	* 10	NS 8	NS 4	NS 8	NS 9	* 10
	D	** 13	** 16	** 15	NS 7	** 17	* 11
	E	** 14	** 12	** 12	* 11	* 10	* 9
	F	** 13	* 9	** 13	** 12	** 13	NS 6

		MATH					
REST	Microstate	A	B	C	D	E	F
	A	NS 6	** 16	** 12	* 10	** 20	** 16
	B	** 15	* 9	** 12	NS 8	NS 9	** 12
	C	* 11	* 11	NS 7	* 11	NS 9	** 12
	D	** 17	** 16	** 17	** 19	** 16	** 12
	E	** 20	** 16	** 21	** 21	** 16	NS 7
	F	** 14	** 13	** 16	** 17	* 21	NS 9

* p < .001 (T>9.5)
 ** p< .0001 (T>12)
 Bonferroni corrected
 Values = Tmax.

Table S1. Result of the T-test across subjects of the sources derived for each microstate in each of the three conditions. Significance values and maximal T-values are given. Note that in general the sources of the microstates with the same label are not significantly different, while the sources of different microstates are. An exception is microstate D and E in the comparison of the math vs. the rest condition. In this case all significantly different solution points for microstate D were located in the superior frontal gyrus where stronger activity was found in the rest condition.

3 General Discussion

3.1 Summary of the main findings

Here, I will first summarize the main findings of the four studies included in this thesis and address some of the open issues. I will integrate results from the studies into a larger context of the recent cognitive neuroscience research and include a short discussion about theories of self-consciousness. I will conclude this chapter by suggesting how future work could incorporate the findings from my thesis to the recent clinical work on memory prosthesis and enhancement.

3.1.1 Bodily-self effect on episodic autobiographical memory (study 1)

In the first study (**study 1**) we investigated how an integration of visual and proprioceptive, multisensory bodily cues influence long-term episodic autobiographical memory. We have showed that the episodic memory for real life-like events may be specifically manipulated by the self-related, bodily cues. This study drew us to make three main conclusions: First, our VR setting enabled us to measure objective memory recognition for real life-like scenes that are immersive and integrating the moving physical body of the participants into these scenes. The VR setting approached naturalistic, real life-like and subjective experiences, yet in a controlled laboratory-based environment. Second, we showed that memory recognition is time-dependent and further relies on the number of changed items between encoding and retrieval. Third, our data revealed that viewing one's own physical body as part of the VR scene during encoding enhanced memory retrieval. Importantly, this body-specific effect was not observed when no-body was presented or when a control object replaced the body. Thus, we argue that *embodied views lead to body-related performance changes*, as described in studies investigating features of bodily self-consciousness. To conclude, in this study we argue that the experience of the physical *bodily-self* is *intrinsically linked to the autobiographical-self*.

3.1.2 The self-experience in bodily consciousness and memory (study 2)

In the second study (**study 2**) we examined how the self-related, multisensory cues from one's own body relate to the subjective re-experiencing of past events, which are usually retrieved from a viewpoint and location similar to encoding. We have shown that episodic autobiographical memory is not only functionally, but also anatomically overlapping with bodily self-consciousness. The present study allowed us to make two major conclusions: First, we show *an anatomical overlap bilaterally in the angular gyrus between bodily self-*

consciousness and episodic autobiographical memory. Multisensory cues about the body, such as proprioception or viewpoint, are usually present during the encoding of personal events. Therefore, we argue that these bodily signals are relevant not only to the bodily self-consciousness, but also to episodic autobiographical memory. Second, we found no anatomical overlap between bodily self-consciousness and semantic autobiographical memory. Consistent with the prior literature that shows that the angular gyrus represents a heterogeneous area comprising functionally and anatomically distinct sub-regions (Daselaar et al., 2013; Hutchinson et al., 2014), we found that semantic autobiographical memory does not anatomically overlap with bodily self-consciousness in lateral parietal cortex. Therefore, we argue that the parietal regions are associated differently with episodic and semantic memories, especially because *semantic autobiographical memory is independent of re-experiencing conscious, vivid and multi-modal life episodes.* To conclude, this study suggests that the conscious re-experiencing of past events and the conscious experience of being located and experiencing the world from first-person perspective depend on the lateral parietal cortex region. Especially, the angular gyrus seems to be involved in processing both the bodily self-consciousness and episodic autobiographical memories. Therefore, we suggest that *the angular gyrus may be the key structure for neural processing related to self-consciousness.*

3.1.3 Retroactive effect of the bodily-self on episodic memory (study 3)

In the third study (**study 3**) we explored how the bodily self-related cues, particularly the presence or absence of one's own physical body from first-person perspective influence the retroactive and selective memory for conceptually related information. We have shown that seemingly insignificant everyday details of neutral real life-like events can be retroactively enhanced, if future conceptually related details acquire significance by the presence of one's own physical body. We have made two major conclusions in this study: First, we replicate our first study, in which we showed that *the presence of one's own physical body enhances the memory for real-life like events.* Instead of using inside rooms, which we have used as our VR paradigm in the study 1, here we have created a novel VR paradigm consisting of outside scenes into which we immersed our participants during the memory stages of encoding and retrieval in order to test the memory performance. Second, we demonstrate that one's own *physical body selectively and retroactively strengthens memory* recognition for items from real life-life events. This result confirms and extends previous studies (Dunsmoor et al., 2015; Patil et al., 2017) by showing that the presence of one's own physical body retroactively enhances memory for real life-like events and that b.) the retroactive memory enhancing can be generalized to

conceptually related items encoded in real life-like scenes. To conclude, we show that *multisensory bodily self-related cues can significantly modify the re-prioritization*, i.e. memory is retained if any information may become relevant in the future, which is a process involving the post-encoding memory consolidation (Tambini et al., 2010, 2017; Tambini and Davachi, 2013; Tompary et al., 2015).

3.1.4 Task-initiated spontaneous thoughts with EEG and fMRI (study 4)

In the fourth study (**study 4**) we examined the temporal structure of self-generated cognition, which is a key attribute to the formation of a meaningful stream of consciousness. Recent fMRI studies suggested that functionally distinct subsystems of the default mode network are activated *at the same time* during task-initiated self-generated processing, seemingly in contradiction with overwhelming evidence that information processing evolves through a stream of *discrete* conscious units. We used ultra-high field functional magnetic resonance imaging and high-density electroencephalography to analyze the continuous thoughts of participants, who were instructed to retrieve self-relevant past events. EEG microstate analysis allowed us to examine these short-lasting (i.e. milliseconds scale) participant-focused thoughts. The fMRI data confirmed that distinct subnetworks of the DMN are concurrently activated during episodic memory retrieval; however, these subnetworks were markedly separate based on their functional connectivity. Crucially, the EEG microstate analysis showed that these functional networks are temporally parsed. Our findings support an increasing evidence that particular fMRI networks can be observed with EEG microstate method as re-occurring, integrated short-lasting periods of synchronized neuronal activity, which last fractions of seconds. To conclude, we argue that our results offer direct evidence that the resting state networks captured by fMRI are closely linked to repeated occurrence and prolongation of mental *states of synchronized neuronal activity* as demonstrated by EEG microstates.

3.2 Conclusion and Outlook for future work

3.2.1 Can amnesic patients have a conscious sense of self?

The inner self exists uniquely as a conscious mental state of each person, who is the only one who can access this state. An observer may distinguish various conscious states of others, but the *“self-experience of how it feels”* is restricted to the inner self of the involved person. As James (1890) described, *“when I wake up, I do not have to question “who am I”, because I still have my own thoughts that seem to be continuous and represent my personal past.”* One may assume that others have similar inner experiences, but nobody else can directly experience the inner self of others. Consciousness is detectable in behavior of others, but none of the neuroimaging techniques can fully read the mind of private thoughts (Lee and Kuhl, 2016; Wang et al., 2017). Some philosophers and neuroscientists have argued that without memory, we lack the sense of self and our personal identity. Our sense of self includes the story of our past and imagining the future (Tulving, 1985). Ascribing consciousness to those who cannot talk about their experiences, such as infants (Kouider et al., 2013) or severely brain injured patients (Owen et al., 2008), is more difficult. What about the amnesic patient H.M. - did he have a sense of self? Corkin (2013) clearly stated that *“There is no doubt that Henry did have a sense of self, even though it was a fragmented one.”* Patient H.M. was missing the pieces to retrieve any self-relevant experiences or imagine his future, due to his inability to mentally travel in personal time. He lost his ability to remember. Despite his amnesia, he had a sense of self, he remained friendly and intelligent. Patient H.M.’s sense of identity was based on his general knowledge about the world, yet he still had his own beliefs and values. This is in agreement with the studies presented in this thesis. Particularly, in **studies 1, 2 and 3** I have argued that the subjective re-experiencing of past events is usually described as from a viewpoint and location similar to encoding. When patient H.M. was asked about his age, he often missed it by decades and his knowledge about his physical look was full of gaps. Yet, when he looked into the mirror, he seemed to accept the person he saw looking back at him. In the introduction of this thesis, I have presented a study during which patient H.M. was able to recognize a set of complex pictures, based on his sense of familiarity without explicitly recalling having seen them. The declarative memory of patient H.M. was deficient, yet he was left with a vague sense of familiarity that helped him to cope with his amnesia. I would argue that the preserved sense of familiarity corresponds well to the intact parietal regions of patient H.M.

3.2.2 Discrete states of self and their manipulation

Patient H.M. lived 55 years without any possibility to mentally travel consciously back in time or project himself in the future, he was fully trapped in the present moment of his short-term memory span, lasting 30 seconds. When we watch a movie, an entire lifetime can be presented continuously in two hours without anyone feeling that something is missing. Patient H.M. could not construct a continuous autobiography of his own life, because he was not able to create and store any new long-lasting memories. Our long-term memories are critical for survival; however, memories often keep us locked into the identities we have created for ourselves. We replay moments and events that happened before and imagine what might happen in the future, becoming wrapped in emotions and anxieties of these possible events. In **study 4**, I have presented the analysis of EEG microstates, which suggest that the human brain does not process information continuously over time, but rather processes *the information in distinct temporal epochs* (Lehmann et al., 1998). The momentary experience of conscious awareness seems to be homogeneous and indivisible, yet the contents of consciousness are separable entities. In the study, we have argued that EEG microstates may indeed integrate the discrete, temporal units of conscious self-experience into a sequence of consciously experienced inner thoughts.

Understanding the neuronal architecture that forms conscious experiences is one of the essential questions of neuroscience. Why are we conscious? Recent experimental studies have focused on establishing a link between subjective conscious experiences and measurable neuronal activity (e.g., Faivre et al., 2017; Park et al., 2016). “*The easy problem*” is to explain how our brains enable us to perform different tasks (e.g., recognizing sounds, describing our feelings, focusing our attention, making plans or performing movements), such as I examined in **studies 1, 2 and 3**. “*The hard problem*” is to explain why we have subjective experiences at all. How can the human brain give rise to an inner, personal life? The brain generates experiences day after day. A number of researchers have tried to establish a theory of consciousness, such as the *Global neuronal workspace* (Dehaene et al., 1998) and *Information Integration Theory* (Tononi et al., 2016) that could predict under which conditions any particular system may have an experience.

The *Global neuronal workspace* argues that consciousness emerges when workspace neurons from a number of a brain regions become co-activated from discrete spatio-temporal patterns of global activity. The network of neurons that transmits information is hypothesized to be situated in the frontal and parietal lobes. Once the information is transmitted on the network

and globally available, the information becomes available and a subject may become consciously aware of it. The *Integrated information theory* (Tononi et al., 2016) suggests that each experience has particular essential properties: intrinsic, existing only for the subject, structured and specific, distinct from any other conscious experience, unified and definite. In agreement with both the Global neuronal workspace and Integrated information theory, I have argued in **study 4** that EEG microstates are the electrophysiological correlates of a global brain integration. The time window during which spatially distinct brain processes are accepted as a momentary EEG microstate lasts between 75 and 150ms (Koenig et al., 2002). Interestingly, a number of theories propose that consciousness may be parceled into discrete states lasting around 100 ms (Baars, 1997; Deco et al., 2011; Efron, 1970; Rabinovich et al., 2001). Thus, it seems intriguing to consider that the electrophysiological EEG microstates may reflect *the building blocks of consciousness* (Baars, 2002b; Changeux and Michel, 2004).

A number of previous studies have tried to relate EEG microstates to the ongoing mental activity. For example, Seitzman and colleagues (2016) altered the temporal features of the 4 canonical microstates by instructing their participants to either mentally subtract numbers or to spontaneously mind-wander. They found significant decrease in occurrence and duration of microstate C and increase in microstate D during mental calculation, supporting the hypothesis that this state is related to externally-oriented, attentional system. The study of Milz and colleagues (2016) showed an increase in microstate A while visualizing and microstate B while verbalizing. Thus, these studies show that the temporal dynamics of EEG microstates may be sensitive to instruction and changes in the content of spontaneous mentation. Furthermore, it could be argued that if EEG microstates are perceptive of the level of consciousness, then they should be modulated by changes of the state of mind. The study of Panda and colleagues (2016) recorded simultaneous EEG-fMRI while experienced participants meditated. This study showed that at rest, the meditators exhibited increased duration and occurrence of default mode network related microstate C, which further increased during meditation.

A more precise definition of EEG microstates and further understanding of their functional role as well as clinical relevance is still needed. A recent meta-analysis on EEG microstates (Rieger, 2016) showed that the default mode network-related microstate C increased in occurrence in patients with schizophrenia, who suffer from an exaggerated sense of self. Contrary to schizophrenia, reduced occurrence of EEG microstate C has been observed in dementia patients (Nishida et al., 2013). Similarly, findings from fMRI studies show that the default mode network connectivity increases in schizophrenic patients (Whitfield-Gabrieli and Ford, 2012),

decreases in vegetative patients and coma and disappears in brain death (Vanhaudenhuyse et al., 2010). Therefore it seems that default mode network is involved in self-consciousness (Fingelkurts and Fingelkurts, 2011). Does it mean that the self disappears once we die (Pereira et al., 2015)?

3.3.3 Memory enhancement and memory prosthesis

Autobiographical memories are the vivid and rich recollections of our lives, which essentially shape who we are (Tulving, 2002b). Loss of autobiographic memory, among the first symptoms reported by patients suffering from Alzheimer's disease (AD), is one of the most devastating conditions, which affects considerably the quality of everyday living. While non-invasive techniques are gradually allowing the theoretical examination of how memories are encoded and retrieved, the *transition from basic science to clinical application* is still highly challenging. AD is the leading cause of dementia, affecting approx. 50 million people world-wide. AD is also the leading cause of disability amongst older people and the 6th leading cause of death. Despite this enormous disease burden, therapeutic options are very limited. The neural circuitry of the brain's memory network still keeps many mysteries. While there are pharmacological interventions that *transiently improve* cognitive function, there are no treatments that *alter* disease progression. Neuroimaging data are *correlational* and as such cannot provide *direct, causal links* between brain activity and memory performance. Similarly, neuropsychological studies often include *unique symptoms* of individual patients and thus require caution when making generalized conclusions. Thus, other non-invasive techniques may be better suited to overcome these limitations. As such, the development of a disease-modifying intervention would be of great clinical significance.

Targeted non-invasive electromagnetic brain stimulation has been applied to *directly enhance* episodic memory in healthy participants. Wang and colleagues (2014) used multiple sessions of high-frequency repetitive transcranial magnetic stimulation (rTMS) over the posterior parietal cortex and demonstrated increased functional connectivity among cortical-hippocampal network regions, including the precuneus, parahippocampal cortex, superior parietal cortex and left lateral parietal cortex. Furthermore, changes in fMRI connectivity were correlated with increase in associative memory (i.e. face-word cued recall) performance. The same group (Nilakantan et al., 2017) later tested the effects of multiple sessions rTMS and showed that the left lateral posterior parietal cortex targeted stimulation enhanced precise memory details (i.e. object-location memory task). Recent rTMS study (Wang et al., 2018)

revealed boosting of semantic memory representation and showed the impact of stimulation on the neural substrates of episodic memory. Thus, these facilitatory TMS studies suggest that this non-invasive technique may have an effect on deeply located hippocampal structures without any surgery.

For the past two decades, neuroscientists have been treating neurological disorders with deep brain stimulation (Holtzheimer and Mayberg, 2011), an invasive technique in which electrodes, implanted into specific brain regions, send electrical impulses through targeted neural circuitry. More recently, there has been a gradual progress from using non-invasive TMS in an effort to target the right pathways and help the brain to restore past *memories*, however with inconsistent findings (Suthana and Fried, 2014). Recently, researchers have aimed to develop a *memory prosthesis brain implant* to help patients suffering with memory loss. Ezzyat et al. (2017) used targeted electrical stimulation in epileptic patients with intracranial electrodes to modulate the neural encoding states and subsequent memory outcomes. They suggested that DBS treatment would improve its effectiveness if *the electrical stimulation were applied as a response to particular brain states*, i.e. *closed-loop* approach in which electrodes monitor brain activity and use stimulation centred on neural feedback. The authors emphasized that *memory is a distributed network* and as such *the brain state* of the healthy participant or patient, targeting the right place at the right time, is crucially important in showing the effect of memory improvement. First, they trained multivariate classifiers to identify the unique patterns of brain activity of subject-specific model that could predict whether encoded states would be later forgotten or remembered. For this, they developed a machine-learning algorithm to build a *memory model* suitable to each participant. It could read a patient's neural response and even more specifically, change patterns of low- and high-frequency activity throughout the memory network during the initial presentation of words and as such predict how likely the participants would remember the words later during retrieval. Second, targeted stimulation during learning was applied to electrodes in the memory network nodes. The electrical stimulation enlarged the encoding state and recall if sent when the classifier reported low encoding efficiency. However, when applying the electrical stimulation when the classifier indicated high encoding efficiency, the memory recall was decreased. Thus, this study suggests that using brain-state decoding could increase the possibility to enhance memory. A year later, a similar study from the same group (Ezzyat et al., 2018) used the closed-loop system to stimulate the lateral temporal cortex during a memory task. By developing patient-specific, personalized, machine-learning models, the authors programmed their stimulator to deliver pulses only when memory was predicted to fail. Lateral temporal cortex stimulation enlarged the likelihood of recall by 15 per cent. Thus,

the authors concluded that by linking the brain stimulation to ongoing brain rhythms, they were able to reliably enhance memory. These results represent an early step towards novel technologies that could improve memory function in Alzheimer's disease patients.

Hampson et al. (2018) went a step further by demonstrating the first human implementation of a system for restoring memory function by means of the patient's own *hippocampal spatiotemporal neural memory codes*. They used data from the memory task to understand the configurations of brain activity associated with individuals' memory performances. Later, they made the device electrically stimulate similar brain activity in the participants while they performed further memory tasks. Memory performance improved by 35 per cent when using the correct stimulation pattern, while random stimulation impaired performance. In conclusion, this memory prosthesis was intended to bypass a damaged hippocampal part and deliver the correctly translated memory to the next brain area by giving small electric shocks to the hippocampus. The group envisions to restore the ability to create long-term memories by implanting silicon chips to mimic the signal processing that neurons perform when they are functioning properly in the brain, allowing to recall past experiences.

A number of open questions arise from these recent studies and their results. Would using non-invasive, rather than invasive, brain stimulation techniques find the same results? With regard to the studies presented in this thesis, how can this stimulation method ensure that people selectively remember what's significant in real life-like rather than laboratory-based settings? How can we ensure that the right memories are enhanced? Would a replication in more patients and with diseases such as dementia show the same results? Is this the first step towards "*a personal memory pacemaker*"? Thus, more work is needed toward the long-term vision of restoring memory function.

3.3.4 Concluding remarks

In conclusion, self-consciousness has been considered by philosophers, psychiatrists, psychologists and recently also cognitive neuroscientists as one of the most astonishing characteristics of the human brain. Self and self-consciousness are difficult to define as they include a number of different concepts, such as *physical self* or *autobiographical self* (Damasio, 1999; Riva, 2018). As described in the introduction, the fundamental aspects of the self and its link with the body, the so-called bodily self-consciousness, have been recently investigated (Blanke, 2012; Serino et al., 2015). Conscious experiences are not always specifically bound to here and now. The subjective experience of mentally travelling back in time or projecting oneself in the future has been associated with the autonoetic consciousness, which is the key feature of episodic autobiographical memory (Tulving, 1985). In this thesis, I have examined how the sense of bodily-self relates to the autobiographical sense of self. Furthermore, I have studied how to experimentally capture the brief periods of personal, inner conscious experiences. In order to investigate the underlying aspects of self-consciousness and its relation to memory and body, a number of cognitive neuroscience approaches, including virtual reality (VR), electroencephalography (EEG) and functional magnetic resonance (fMRI), have been employed in this thesis. **Study 1** investigated how the presence or absence of *multisensory bodily cues influence episodic autobiographical memory*. In this study, we have used a novel immersive VR system in order to create highly controllable lab-based setting, which would imitate the naturalistic environment of everyday life events. **Study 2** examined *the neural mechanisms underlying the bodily and autobiographical self*. In this study, we have combined the results from a recent publication of Ionta et al. (2011), which showed that the inferior parietal lobule was associated with some of the key aspects of the bodily self-consciousness, with a meta-analytically based investigation of episodic and semantic autobiographical memories. **Study 3** explored the advantages of our immersive VR system to *selectively and retroactively enhance episodic autobiographical memory*. By manipulating the presence or absence of one's own body, we reported changes in post-encoding memory consolidation. **Study 4** applied the recent fMRI and EEG methods to capture the inner, personal conscious mentation. In this study, we have shown that it is possible *to manipulate and enhance specific, inner thoughts*. Finally, the long-term vision of the memory research should try to bridge the existing gap between basic and translational neuroscience by improving the early diagnosis, long-term treatment for the early stages of memory loss and modern technology which could produce meaningful gains in memory performance.

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5 Abbreviations

1PP	first-person perspective
3PP	third-person perspective
ALE	activation likelihood estimation
BA	Brodmann area
BSC	bodily self-consciousness
DBS	deep brain stimulation
EAM	episodic autobiographical memory
EEG	electroencephalography
HMD	head mounted display
fMRI	functional magnetic resonance
OBE	out-of-body experience
RHI	rubber hand illusion
TMS	transcranial magnetic stimulation
VR	virtual reality

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Languages:

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Teaching Assistant:

2017-present MOOC: Fundamentals of Biomedical Imaging: Magnetic Resonance Imaging
2017-present MOOC: Fundamentals of Biomedical Imaging: Ultrasounds, X-ray, positron emission tomography (PET) and applications
2014-2016 MSc course, EPFL: Behavioral and Cognitive Neuroscience
2014-2016 BSc course, EPFL: Neuroscience for Engineers

Scientific Supervision:

Title of the project	Type of Supervision	Length
OHBM International Online Mentoring	BSc and MSc Mentoring	1.1.2018-present
“Retroactive Strengthening of Memory”	BSc Project in Life Science	8.8.-2.9.2016
“Influence of exteroceptive and interoceptive signals on the episodic memory”	BSc Project in Life Science	1.2-6.2. 2016
“Self-Memories and Virtual Reality”	MSc Project in Bioengineering	16.2.-19.6.2015
“Influence of Body on Memory”	High School visitor	12.9.-23.9.2015

Institutional Responsibilities and Work Experience:

2016 Brain Stimulation and Imaging Meeting, Geneva, help with organization
2016-2017 Scientific Guide at the Exposition “Pas de Panique”, Geneva
2015-2016 Managing The Recruiting System of Participants at Campus Biotech, Geneva
2013 fMRI operator training, Brain & Behavior Laboratory (BBL)
2008-2009 Fairtrade committee, St. John’s College, Durham
July 2008 Cambridge Scholars Network, Downing College, Cambridge- coordinator
2007-2008 School of Theology, Tyndale House, Cambridge- internship, coordinator
August 2007 Apologetics Course, Sidney Sussex College, University of Cambridge

AWARDS:

Selected Article highlighting multi-modal (EEG-fMRI) imaging	Campus Biotech	June, 2018	Geneva, Switzerland
Best Oral Presentation	Springer	9.1. 2017	Champéry, Switzerland

Membership:

2018-	member of The International Society for Brain Electromagnetic Topography
2014-	member of the Organization of Human Brain Mapping (OHBM)
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2008-2009	Theology Network, Durham (UCCF)

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Bréchet, L., Mange, R., Herbelin, B., Gauthier, B., Serino, A., Blanke, O. (2018). Viewing one's body during encoding boosts episodic memory. Under review after 1st revision in *PlosOne*. Preprint published in: bioRxiv, doi: <https://doi.org/10.1101/318956>.

Bréchet, L., Grivaz, P., Gauthier, B., Blanke, O. (2018). Common recruitment of angular gyrus in episodic autobiographical memory and bodily self-consciousness. In press in *Frontiers in Behavioral Neurosciences*. Preprint published in: bioRxiv, doi: <https://www.biorxiv.org/content/early/2018/06/14/345991>.

Bréchet, L., Brunet, D., Birot, G., Gruetter, R., Michel, CM, Jorge, J. (2018). Capturing the spatiotemporal dynamics of task-initiated thoughts with combined EEG and fMRI. Under review in *Neuroimage*. Preprint published in: bioRxiv, doi: <https://www.biorxiv.org/content/early/2018/06/14/346346>.

Bréchet, L., Hausmann, S., Mange, R., Blanke, O., Serino, A. The Bodily Self Selectively and Retroactively Strengthens Episodic Autobiographical Memories During Post-Encoding Consolidation. (*in preparation*)

Jorge, J., Boulouc, C., **Bréchet, L.,** Michel, CM., Gruetter, R. (2018). Investigating the variability of cardiac pulse artifacts across heartbeats in simultaneous EEG-fMRI recordings: a 7T study. Under review in *Neuroimage*.

Invited Talks and Oral Presentations:

Title	Type of Contribution	Date	Place
Sixth Biennial Conference on Brain Connectivity	Poster	24.-25.9.2018	Montreal, Canada
Limitless! Augmenting Brain Function	Poster	19.-21.8.2018	Lausanne, Switzerland
Human Brain Mapping Annual Meeting	Poster	17.-21.6. 2018	Singapore
BBL/CIBM Research Day	Poster	6.6.2018	Geneva, Switzerland

Swiss Society for Neuroscience	Poster	9.2. 2018	Zurich, Switzerland
BMI-NCCR Synapsy Meeting “Neurobiology of Mental Health”	Poster	24.-26.1. 2018	Geneva, Switzerland
Alpine Brain Imaging Meeting	Oral Presentation	7.-11.1.2018	Champéry, Switzerland
Brain and Mind Symposium	Poster	16.-17.11.2017	Lausanne, Switzerland
Campus Biotech Human Neuroscience	Oral Presentation	6.11.2017	Geneva, Switzerland
EEG-fMRI OHBM Symposium	Poster	3.-4.11.2017	Bern, Switzerland
Technical Institute CEITEC	Invited talk	24.10.2017	Brno, Czech Republic
Brain Stimulation and Imaging Meeting	Poster	23-24.6.2017	Vancouver, Canada
International Conference on Memory	Poster	17-22.7.2016	Budapest, Hungary
Human Brain Mapping Annual Meeting	Poster	26.-30.6. 2016	Geneva, Switzerland
Brain Stimulation and Imaging Meeting	help with organization	24-25.6.2016	Geneva, Switzerland
LNCO Annual Retreat	Oral Presentation	15-18.6.2016	Stresa, Italy
The Brain Forum	Exhibitor & Poster	26.-27.5. 2016	Lausanne, Switzerland
Campus Biotech Human Neuroscience	Oral Presentation	2.5.2016	Geneva, Switzerland
Center for Neuroprosthetics Annual Retreat	Poster	25-26.1. 2016	Chamonix, France
Swiss Society for Neuroscience	Poster	23.1. 2016	Lausanne, Switzerland
Alpine Brain Imaging Meeting	Poster	11-16.1.2016	Champéry, Switzerland
BMI-NCCR SYNAPSY: “Mechanisms of Memory Consolidation, Reconsolidation and Extinction”	Poster	21-22.12.2015	Lausanne, Switzerland
Lemanic Neuroscience Annual Meeting	Poster	28.-29.8.2015	Diablerets, Switzerland
Swiss Memory Workshop	Poster	24-26.8.2015	Spiez, Switzerland
An Interdisciplinary Summer School: “The Social Self: How Social interactions shape body and self-representations”	Oral Presentation	21-27.6.2015	Aegina, Greece

