Event structured cognition: the role of event boundaries

Marta Marques de Almeida e Silva

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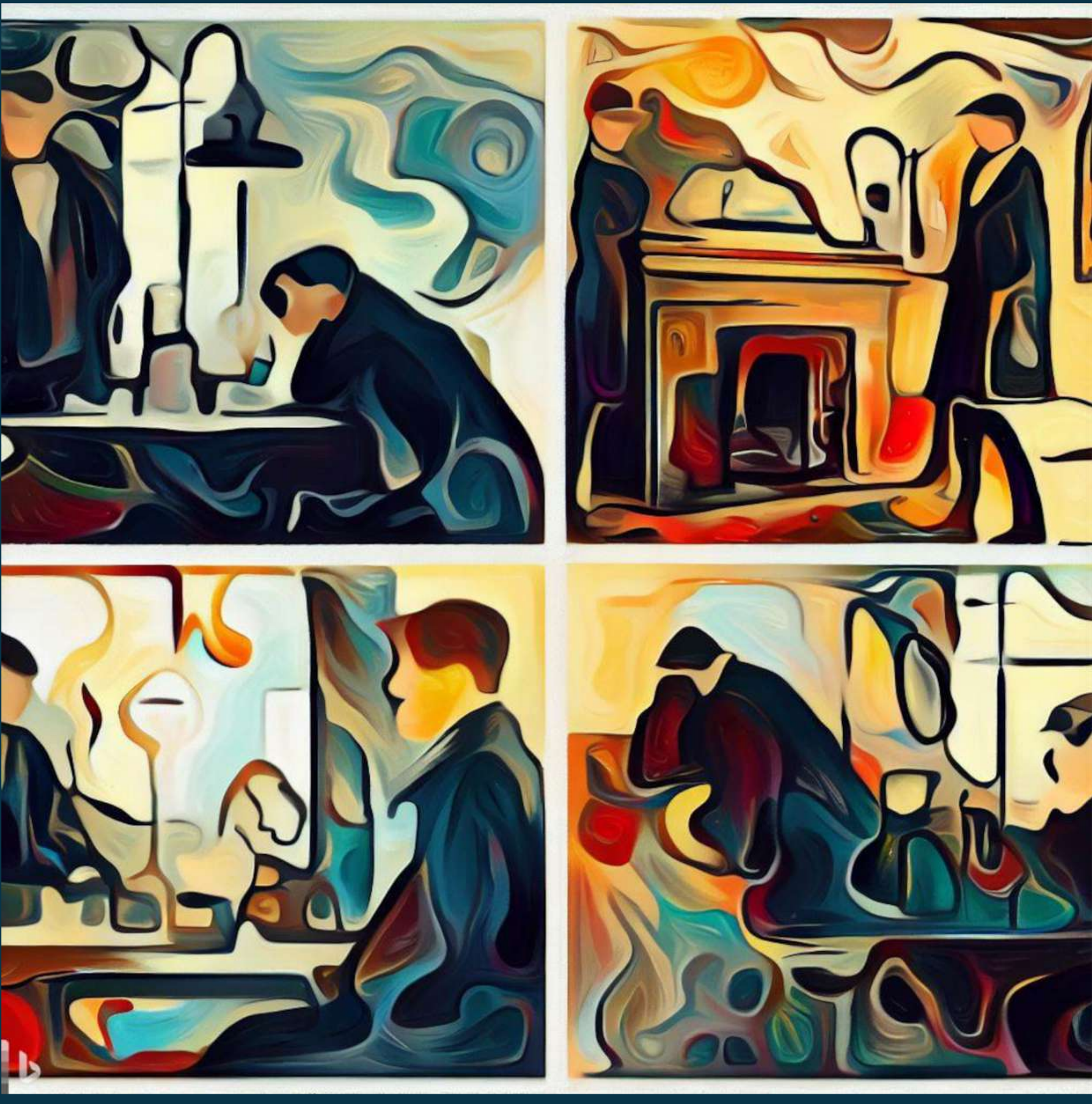

PhD Thesis

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Event structured cognition:

the role of event boundaries

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"la Caixa" Foundation

MINISTERIO DE CIENCIA E INNOVACIÓN

AGENCIA ESTATAL DE INVESTIGACIÓN

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List of Abbreviations

fMRI Functional Magnetic Resonance Imaging

EEG Electroencephalography

MTL Medial Temporal Lobe

EST Event Segmentation Theory

TRW Temporal receptive window

ECoG Electrocorticography

SMSC Standard Model of Systems Consolidation

MTT Multiple Trace Theory

CTT Competitive Trace Theory

SWR Sharp-Wave Ripples

LFP Local Field Potentials

mPFC Medial Prefrontal Cortex

MEG Magnetoencephalography

ERP Event Related Potential

sLORETA Low-resolution Tomography Analysis

HMM Hidden-Markov Model

IED Interictal Epileptiform Discharge

IRI Inter-Ripple Interval

ITPC Inter-Tiral Phase Coherence

PSTH Peristimulus Time Histogram

FDR False Discovery Rate

ICA Independent Component Analysis

LDA Linear Discriminant Analysis

DMN Default Mode Network

RL Reinforcement Learning

Abstract

Since the moment of our birth, we are driven by an insatiable urge to understand and make sense of the world around us. To navigate the continuous flow of experiences, our minds instinctively break them down into discrete events, allowing us to grasp and remember them more effectively. In my PhD research, I delve into this fascinating process, aiming to unravel how the brain's organization of ongoing activity is influenced by the presence of event boundaries—specifically, the beginning and end points of events.

When an event boundary occurs, it serves as a natural break in the stream of experiences, allowing for the encoding and storage of the preceding event as a distinct episode. They may also provide natural breakpoints for evaluation and anticipation. As individuals approach an event boundary, their cognitive systems engage in predictive processing, generating expectations about what might occur next. However, a number of intriguing questions remain regarding the mechanisms behind the detection and segmentation of events. What are the neural processes that allow us to perceive and demarcate event boundaries? How do event boundaries influence the consolidation of memories? How do event boundaries affect the retrieval and evaluation of relevant memories when making decisions?

To investigate these questions, I leverage the remarkable temporal precision offered by electrophysiological recordings conducted on a cohort of healthy participants. Additionally, I tap into the unique opportunity provided by intracranial electroencephalographic recordings obtained from individuals diagnosed with epilepsy, which offer an unprecedented level of anatomical precision. In this thesis research, I have made several noteworthy findings:

Firstly, in Study 1, I discovered that our brains perceive and store information in the form of discrete events. This process occurs rapidly after the conclusion of each event, and it is predictive of later reinstatement or recall of those events. These results provide the first neurophysiological underpinnings for how the memory systems segment a continuous long stream of experience into episodic events.

Secondly, in Study 2, I observed a noteworthy interaction between cortico-hippocampal ripples throughout the encoding of an event, indicating the potential role of ripples in facilitating the integration of diverse memory elements across cortical regions. Moreover, the study found an increase in ripple activity at hippocampal event boundaries. These findings contribute to a deeper understanding of memory encoding mechanisms and emphasize the involvement of ripples in event segmentation.

Thirdly, in Study 3, I found evidence that event boundaries are instrumental in organizing state-space knowledge into a high-dimensional structure when individuals engage in goal-directed behavior. This suggests that event boundaries serve as cognitive anchors that allow us to effectively navigate and manipulate information within a specific context, facilitating adaptive decision making.

By addressing these questions, my research enhances our understanding of the mechanisms underlying event segmentation, memory formation, and decision making. It explores the neural substrates, cognitive processes, and behavioral consequences associated with event boundaries, ultimately shedding light on the fundamental principles governing human cognition. In doing so, we lay the groundwork for future research exploring the intricate interplay between events, memory, and decision making.

Keywords: Electroencephalography, brain, memory, decision-making, event segmentation, boundary, sharp-wave ripples.

Resumen

Desde el momento de nuestro nacimiento, somos impulsados por un deseo insaciable de comprender y dar sentido al mundo que nos rodea. Para navegar por el flujo continuo de experiencias, nuestras mentes ínsitamente las descomponen en eventos discretos, lo que nos permite comprender y recordar de manera más efectiva. En mi investigación de doctorado, profundizo este fascinante proceso con el objetivo de desentrañar cómo la organización de la actividad cerebral se ve influenciada por la presencia de límites entre eventos, específicamente los puntos de inicio y fin de los eventos.

Cuando ocurre un límite de evento, este funciona como una interrupción natural en el flujo de experiencias, permitiendo la codificación y el almacenamiento del evento anterior como un episodio distinto. Además, proporcionan puntos de interrupción naturales para la evaluación y la anticipación. A medida que nos acercamos al límite de un evento, nuestros sistemas cognitivos se involucran en el procesamiento predictivo, generando expectativas sobre lo que podría ocurrir a continuación. Sin embargo, aún quedan preguntas intrigantes sobre los mecanismos detrás de la detección y segmentación de eventos. ¿Cuáles son los procesos neuronales que nos permiten percibir y delimitar los límites de eventos? ¿Cómo influyen los límites de eventos en la consolidación de la memoria de un evento? ¿Cómo afectan los límites de eventos a la recuperación y evaluación de memorias relevantes al tomar decisiones?

Para investigar estas preguntas, aprovecho la notable precisión temporal ofrecida por los registros electrofisiológicos realizados en un grupo de participantes sanos. Además, aprovechando la oportunidad única proporcionada por el registro electrofisiológicos de electrodos intracraneales obtenidos de individuos diagnosticados con epilepsia, que ofrecen un nivel sin precedentes de precisión anatómica. En esta investigación doctoral, he realizado varios hallazgos destacados aquí:

En primer lugar, en el Estudio 1, descubrí que nuestros cerebros perciben y almacenan información en forma de eventos discretos. Este proceso ocurre rápidamente después de la conclusión de cada evento y es predictivo de la reinstalación o recuerdo posterior de esos eventos. Estos resultados proporcionan los primeros fundamentos neurofisiológicos sobre cómo los sistemas de memoria segmentan un flujo continuo y largo de experiencias en eventos episódicos.

En segundo lugar, en el Estudio 2, observé una notable interacción entre las ondas de oscilaciones cortico-hipocampales durante la codificación de un evento, lo que indica el potencial papel de ripples en facilitar la integración de diversos elementos de memoria en regiones corticales. Además, el estudio encontró un aumento en la actividad de este tipo de oscilaciones en los límites de los eventos en el hipocampo. Estos hallazgos contribuyen a una comprensión más profunda de los mecanismos de codificación de la memoria y enfatizan la participación de los ripples en la segmentación de eventos.

En tercer lugar, en el Estudio 3, encontré pruebas convincentes de que los límites de eventos son fundamentales para organizar el conocimiento del espacio de estados en una estructura de alta dimensionalidad cuando las personas se dedican a comportamientos dirigidos por metas. Esto sugiere que los límites de eventos sirven como puntos de referencia cognitivos que nos permiten navegar y manipular efectivamente la información dentro de un contexto específico, facilitando la toma de decisiones adaptativas.

Al abordar estas preguntas, mi investigación mejora nuestra comprensión de los mecanismos subyacentes a la segmentación de eventos, la formación de la memoria y la toma de decisiones. Explora los sustratos neuronales, los procesos cognitivos y las consecuencias conductuales asociadas con los límites de eventos, arrojando luz sobre los principios fundamentales que rigen la cognición humana. Al hacerlo, sentamos las bases para futuras investigaciones que exploren la intrincada interacción entre eventos, memoria y toma de decisiones.

Palabras clave: Electroencefalograma, cerebro, memoria, toma de decisión, segmentación en eventos, frontera, sharp-wave ripples.

Chapter 1

Introduction

1.1 The multidimensional nature of memory

Memories are reflected in thoughts, experiences and behaviors. They influence how we shape our actions even when we are not conscious that they do so. Consciously or not, memory itself is influenced by the past, it is needed to carry our present daily affairs and is extremely important to plan our future.

The day-to-day experiences that are captured in our memories are not isolated snapshots frozen in time, but rather intricate tapestries woven from a multitude of sensory inputs, emotions, and cognitive processes. When we think back to a particular event or recollect a past encounter, we are transported back to a dynamic and multisensory experience. Our memories are not limited to visual images alone but also encompass a symphony of sounds, a kaleidoscope of colors, the aroma of a place, the touch of an object, and even the taste of a dish. These rich sensory details intertwine with the emotional context of the moment, adding depth and meaning to our recollections. Moreover, memories are not confined to a linear narrative structure but instead unfold in a multidimensional fashion. We often recall fragments, snippets, and flashes of events, which may be rearranged and reconstructed over time. The fluid nature of memory allows for the integration of new information and the formation of associations between different experiences. This interconnectedness enables us to draw upon past knowledge, make connections, and engage in creative thinking.

Attempting to unravel the complexities of memory has been a central pursuit in neuroscience. Scientists have made significant progress in understanding various aspects of memory formation, storage, and retrieval, yet many mysteries persist. The brain's intricate network of neurons and their synaptic connections form the foundation of memory processes. Through the strengthening or weakening of these connections, memories are encoded, consolidated, and retrieved. However, the precise mechanisms by which memories are stored and retrieved are still being explored.

Furthermore, the dynamic nature of memory adds another layer of complexity to its study. Memories can be modified, distorted, and even forgotten over time. Factors such as emotions, attention, and subsequent experiences can influence the way memories are stored and recalled.

In conclusion, the day-to-day experiences we remember are intricate and multifaceted, encompassing a rich amalgama of sensory inputs and emotional contexts. Understanding how memory works is an ongoing scientific endeavor, as its complexity presents numerous challenges. The nonlinear, multidimensional, and ever-changing nature of memory requires a comprehensive exploration of the brain's neural mechanisms, the interplay between different brain regions, and the influence of various factors on memory formation and retrieval. By unraveling these mysteries, we can gain deeper insights into the nature of human cognition and the extraordinary capacity of our minds to store and recollect the myriad experiences that shape our lives.

The advances in the field of memory research have been closely intertwined with significant technological breakthroughs and shifts in the scientific method throughout history. The emergence of neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), has played a pivotal role in our understanding of memory processes. These imaging tools have provided researchers with the ability to observe and investigate how memories form, consolidate, and get reinstated within the intricate neural networks of the brain. By mapping the neural substrates associated with memory formation, these techniques have allowed scientists to move beyond mere assumptions about behavior and delve into the underlying mechanisms that shape our memory.

In recent years, there has been a concerted effort among neuroscientists to incorporate more naturalistic stimuli and less simplistic experimental settings into their studies. Recognizing the limitations of traditional laboratory-based experiments, researchers have embraced the importance of studying memory formation in the context of everyday activities. By utilizing real-world scenarios and more ecologically valid tasks, we aim to gain a deeper understanding of how memories are formed and encoded during our daily lives. This shift towards more naturalistic approaches is also driven by the need to place memory within more integrated models of cognition and brain function, recognizing that memory is intricately intertwined with other cognitive processes.

The scope of the thesis presented here aligns with this evolving trend in memory research. By integrating cutting-edge neuroimaging techniques, insights from naturalistic stimuli, and experimental settings that mimic real-life situations, this work aims to shed light on the complex processes that govern memory and contribute to our broader understanding of human cognition and brain function. Through these efforts, we hope to contribute to the ongoing quest for unraveling the mysteries of memory and uncovering the fundamental workings of the human mind.

1.2 Episodic Memory and our continuous experiences

Memory can be categorized into different types based on various factors. These distinctions help us understand the different stages and types of memory involved in processing and storing information. A major distinction can initially be made by distinguishing between short and long-term memory, based on the amount of time the memory can be retained (Tulving 1972; Figure 1.1).

Short-term memory is responsible for storing information temporarily and determining if it will be dismissed or transferred to long-term memory. This term is often used interchangeably with the term working memory, although technically the latter refers to the whole theoretical framework of structures and processes used for the temporary storage and manipulation of information of which short term memory is just one component (Chai, Abd Hamid, and Abdullah 2018).

Long-term memory is suggested to be anything that someone remembers that happened in more distant periods of time. These memories can last from a few days to many years, have different strengths and merge with other memories. Over the years, several types of long-term memories have been distinguished, although their exact relationship is still a matter of debate.

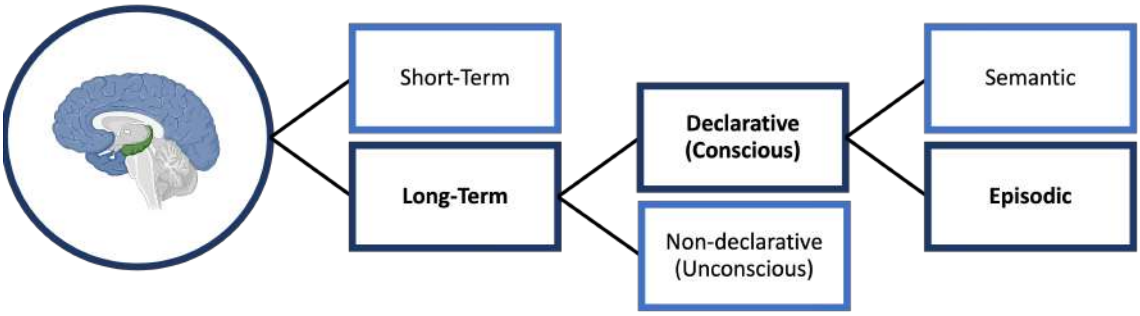


Figure 1.1: Sagital view of the brain with cortex (blue) and hippocampus (green), regions involved in memory processes, and classification of memory types. Declarative memories are believed to be explicit (conscious) and refer to a recollection of facts and events. Non-declarative memory, said to be unconscious, refer to a collection of abilities. Outlined in a darker color and in bold are the types of memories studied in this thesis.

Long-term memories can be considered either declarative (conscious) or non-declarative (unconscious). This distinction has been made evident by the study of patients with brain lesions. Perhaps the most famous one is that of a patient known as 'H.M', who developed a profound amnesia after having parts of his Medial Temporal Lobe (MTL) removed in an attempt to cure his severe epilepsy (Scoville and Milner 1957). The fact that he was able to learn hand-eye coordination skills such as mirror drawing, despite having absolutely no memory of having learned and practiced the task before, suggested the existence of different types of long-term memory (Cohen and Squire 1980). His impairments were mostly present in what has been described as explicit or declarative memory. It refers to memories that can consciously be recalled and can be divided into two subtypes, episodic and semantic (Tulving 1972).

Episodic memory refers to memories that have specific source in time, space, and life circumstances and are often autobiographical in nature, in the way that we can travel mentally back in time to relive the experience (Tulving 1972). Semantic memories involve facts about the world, about ourselves, and about other knowledge that we share with a community (Tulving 1972). Initially memories are believed to be episodic, context-dependent and encoded by the hippocampal complex. Over-time, they can be transformed into semantic memories in the neocortex (Nadel et al. 2000).

A complete conception of human memory entails then the involvement of multiple brain regions, each playing a distinct role in different facets of memory processing. One crucial region is the MTL, which encompasses structures such as the hippocampus, amygdala, and surrounding cortical regions. The hippocampus, in particular, has been extensively studied and is widely recognized as a key player in episodic memory formation. It serves as a hub for integrating information from various sensory and cognitive domains, allowing for the binding of different elements into a coherent memory representation.

While the MTL plays a prominent role in episodic memory, other brain regions within the neocortex, have also been shown to support some aspects of memory (Squire, Cohen, and Zouzounis 1984). The cortex's involvement in memory extends beyond simple storage, as it supports the integration of past experiences with ongoing cognitive tasks, decision-making, and planning (Schacter and Addis 2007).

While we have gained significant insights into the roles of specific brain regions in memory, it is crucial to acknowledge that memory is a complex and distributed process. It involves the intricate interplay of multiple regions, and the specific contributions of each region may vary depending on the type of memory being processed and the contextual demands. Lately research has also been indicating that the processing and storage of memory is not only sensitive to this spatial organization but also to the temporal properties of the stimuli itself, given that what we experience daily contains highly dynamic spatial-temporal properties.

1.3 Event Segmentation: our brain as a movie editor

The information that we experience in our daily life reaches to us in the form of a continuous stream that arrives on a wide range of timescales. As an example, imagine you are attending a bustling marketplace in a vibrant city. As you navigate through the lively stalls, a continuous stream of sensory information bombards you. You hear the chatter of conversations, the calls of vendors, and the melodies of street musicians. The aromas of various cuisines waft through the air, blending with the scents of fresh produce and fragrant flowers. The touch of different textures can be felt as you browse through handmade crafts or sample the textures of various fruits and vegetables. In this bustling marketplace, the continuous stream of information arrives on various timescales. Conversations ebb and flow, with snippets of dialogue catching your ear as you pass by different groups of people. The sounds of vendors promoting their wares and the rhythm of music performances create a symphony of auditory stimuli. The visual information unfolds as you scan the surroundings, taking in the details of each stall, the movement of people, and the interplay of colors and shapes.

As you navigate through this multisensory experience, your brain actively processes and integrates the information, allowing you to interact with your environment. The continuous stream of sensory input shapes your perception of the marketplace, creating a rich and dynamic experience. The memories formed during this encounter are not isolated moments but rather a holistic representation of the sights, sounds, smells, tastes, and tactile sensations that contribute to the vibrant atmosphere of the marketplace. Thus, the importance of the neural mechanisms by which information can be accumulated over time has been increasingly gaining interest on the neuroscience field. It is an intuitive fact that human observers know about the parts of everyday activities, use this information extensively in cognition and can intentionally segment the ongoing activity into different segments. Not only we segment the information we perceive but we also remember things as episodes that represent previous experiences (Kurby and Zacks 2008). But, how do individuals' segment and organize events in real-time, and what factors influence this segmentation process?

Jeffrey M. Zacks and his colleagues initially described an event as “a segment of time at a given location that is perceived by an observer to have a beginning and an end” (Zacks, Tversky, and Iyer 2001). Although useful, this description does not capture the complexity of the event conception. Events are goal-directed human representations of states of the world, with modest duration that can range from seconds to tens of minutes. They allow an organism to anticipate the future and to plan appropriate actions rather than merely react to incoming stimuli.

A few years later the same first author proposed the Event Segmentation Theory (EST) in which perceptual processing is guided by a set of representations called event models that are working memory representations, which are implemented by transient changes in neural activation (Zacks et al. 2007). Periods of stability are then perceived as events and periods of change as the boundaries between events. Event models are multimodal, *i.e.*, they integrate information from different sensory modalities and receive information from semantic memory representations capturing shared features of previously encountered events. The EST was then the first theory to propose event segmentation as a domain-general mechanism of cognitive control due to its potential role not only in perception but also, resource allocation, memory encoding, planning and decision making.

1.3.1 How do we form event memory representations?

Initially, researchers focused on identifying and characterizing the neural dynamics involved in the creation of the event representations. Behavioral studies have shown that subjects can segment events into a nested hierarchy from coarse to fine timescales (*i.e.*, segment either in large or small units, respectively), simply by being asked to do so. For example, when walking into a kitchen to get a glass of water you walk over to the cupboard, remove a glass, turn around, walk to the sink, fill the cup, turn around and walk back to the room you had just came from. Each of these actions could be seen as a discrete event, or they might be classified into one larger unit such as ”getting a glass of water”. Participants in past studies have been asked to watch videos of individuals performing simple tasks as the one I just described, and divide the scene into smaller or larger units. This type of segmentation was shown to be reliable and systematically related to objective features of the stimuli, and predictive of later recollection (Newtson and Engquist 1976; Speer, Swallow, and Zacks 2003). Neuronal imaging evidence of this segmentation hierarchy was also found in a fMRI study where participants watched video depictions of everyday activities and had to press a button to mark the end of events at a coarse and fine temporal grain, with networks of posterior regions showing increased neural activity well before the explicitly identified boundary points (Zacks, Tversky, and Iyer 2001). In light with these findings, EST stated that people do not perceive event boundaries on only one timescale. Rather, they perceive event boundaries on multiple timescales simultaneously, but selectively attend to one specific timescale.

Years later in 2008, Hasson and his colleagues conducted a study to investigate how different areas of the cortex respond to sensory information accumulated over different time scales. They were interested in understanding the temporal dynamics of cortical processing and the persistence of neural responses in different brain regions (Hasson et al. 2008). They discovered a hierarchy of temporal receptive windows (TRW) which are the lengths of time during which sensory information may sustain a brain response (Figure 1.2). Early sensory areas would maintain information only for short durations (short TRWs), enabling rapid processing of the ever-changing sensory input, whereas higher level brain regions, such as the parietal and frontal cortex, maintained information for much longer time (longer TRWs) allowing them to process information from perceptual and cognitive events that unfold over time. A similar TRW hierarchy was found on the auditory and language areas by asking subjects to listen to a real-life story scrambled at the time scales of words, sentences, and paragraphs (Lerner et al. 2011).

A few years later, Honey et al. 2012 hypothesized that regions with longer TRWs would have distinctive properties in their population dynamics, more precisely slow cortical dynamics. This distinct population dynamics may be essential to ensure the accumulation information over longer timescales. Using electrocorticographic (ECoG) recordings they were able to examine the time course of neural activity within broad high-frequency range (64-200Hz) and concluded that regions with longer TRWs exhibited slower fluctuations than power fluctuations at higher portions of the high-frequency band. On the next year, similar observations across the whole cortex using fMRI recordings were made (Stephens, Honey, and Hasson 2013). These results suggested that, not only information is processed in different timescales, but also that the dynamic timescale in each region is determined, in part by intrinsic structural properties.

In an experimental approach where subjects had to watch a 50 min movie, and/or listen to the same narrated story, Baldassano et al. 2017 showed that a number of key regions, later extended to all cortical areas by Geerligs et al. 2022, exhibited a hierarchical event-structured organization. They also found that event boundaries annotated by human observers most strongly related to long events at the top of the hierarchy, independently of the type of stimuli (movie description of the story vs. narrative description).

After the abovementioned studies it was clear that event perception occurs differently throughout the cortex and that these different regions are indeed sensitive to the temporal organization of the stimuli itself. However, which role does this temporal organization play on memory remained unknown.

1.3.2 The role of event boundaries in memory formation

Event segmentation is now known to affect not only our perception of the experience, but its subsequent organization in long-term memory (Kurby and Zacks 2008; Radvansky 2012; Sargent et al. 2013), such that elements within an event are bound together more cohesively than elements across events (Ezzyat and Davachi 2011; DuBrow and Davachi 2013; DuBrow and Davachi 2014; Horner et al. 2016). Indeed, the idea that the organization of our memory takes place online, during encoding, has been established since the conception of the EST (Zacks et al. 2007). According to the EST, perceptual information at event boundaries (*i.e.*, the moments in time where an event ends and a new one starts) receives more extensive processing than perceptual information from other points in time, which would result in better long-term memory for this information.

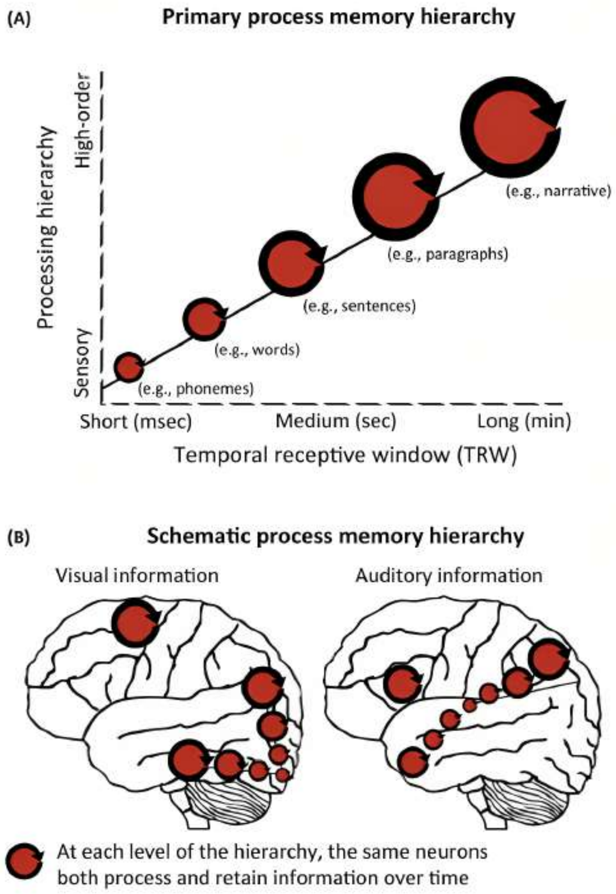


Figure 1.2: (A) A hierarchy of process memory in which in each region the TRWs increase in a topographically organized manner, from milliseconds in sensory areas up to minutes in high order regions. (B) A schematic process memory hierarchy for auditory and visual stimulation. Adapted from Hasson et al. 2008

Indeed, superior recall memory has been observed for information occurring near event boundaries (Newtson and Engquist 1976; Schwan, Garsoffky, and Hesse 2000). Editing movies by deleting intervals containing event boundaries impairs memory for the movies more than deleting portions of the movie that do not coincide with event boundaries (Schwan and Garsoffky 2004). Similarly, inserting commercial breaks or pauses into films at event boundaries can improve memory, and inserting such breaks between event boundaries can impair memory (Boltz 1992; Schwan, Garsoffky, and Hesse 2000). The presence of an event boundary, such as transitioning between different contexts or rooms, diminishes the strength of sequential binding and as a result, individuals are more prone to forgetting the precise order of item pairs that span across these context shifts (DuBrow and Davachi 2013; DuBrow and Davachi 2014; DuBrow and Davachi 2016; Ezzyat and Davachi 2011; Horner et al. 2016).

Event boundaries can also influence our perception of time, specifically by expanding the subjective duration of time. When items span across event boundaries, they are often recalled as occurring further apart in time, even if their actual temporal distance remains the same (Ezzyat and Davachi 2014). Overall, all these findings emphasized the importance of event boundary placement in determining whether/how incoming information becomes integrated into a unified memory representation.

Recent advances in neuroimaging studies have shed new light on the kinds of brain activity that respond to event boundaries and that define 'events' themselves. Particularly, in a study where participants had to watch a movie, and/or listen to the same narrated story and do a free verbal recall, researchers discovered that a selective increase of activity at the hippocampus at event boundaries, with a peak response within several time points after the event boundary (Ben-Yakov and Dudai 2011; Figure 1.3). This post boundary activity in the hippocampus was studied in more detail in a Ben-Yakov and Henson 2018 study, who showed that the hippocampal response was sensitive to boundary strength (quantified as the number of participants that agreed on a given boundary within the film). In a similar movie watching approach Baldassano et al. 2017 showed that this post-event hippocampal activity was related to pattern reinstatement during recall. Although the magnitude of the signal was not directly associated with subsequent memory performance, it was correlated with the duration of free recall, indicating the time participants spent recalling details from the preceding events. This suggests that the post-event hippocampal signal may have represented the extent to which episodic details of the previous event were encoded into long-term memory.

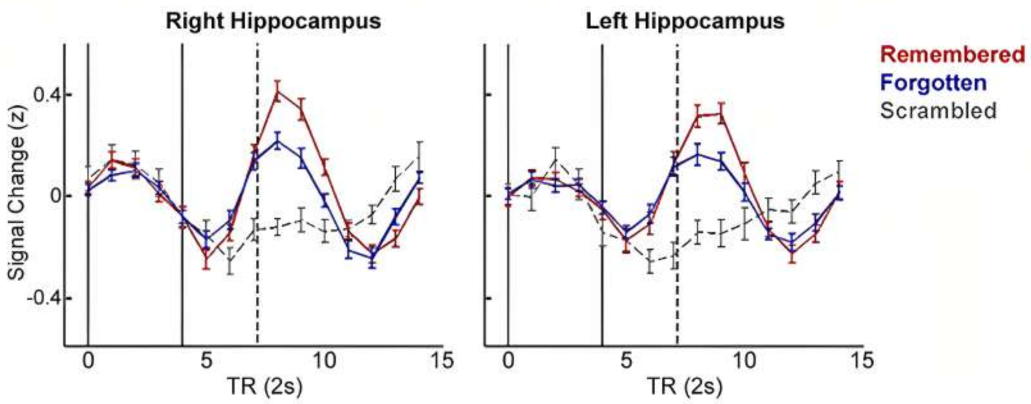


Figure 1.3: The hippocampus responds to event boundaries and is correlated with subsequent memory. Adapted from Ben-Yakov and Dudai 2011.

In an ECoG study, where patients were simply asked to listen to a short-story in two runs, Michelmann et al. 2021 extended the fMRI findings of enhanced hippocampal activity at event boundaries by showing enhanced information flow from cortex to hippocampus, measured using mutual information. The intricate communication between the hippocampus and neocortex is thought to play a pivotal role in the formation of long-term memories Nadel et al. 2000. The end of an event may therefore be an ideal moment to store a coherent representation of the just encoded event before an imminent change in the environment occurs.

Nevertheless, whether this event-offset signal reflects an active rehearsal and re-encoding of recent events was still unclear. The first evidence that just-experienced episodic information may indeed be reactivated at boundaries was shown in a study from Sols et al. 2017. Using pattern similarity analysis on EEG, they found that event boundaries triggered activity associated to the reinstatement of just-experienced information. The degree of similarity between the neural activity elicited by the just encoded episode and the neural activity elicited at the boundary positively correlated with the ability to later link across different sequences of events. These results were the first to suggest that post-event memory reactivation also helps maintaining temporal memory integration across events.

The previously mentioned research suggested that in segmenting our daily life continuous experiences into discrete events, the brain can integrate the information into meaningful episodic structures. This integration seems to take place at event boundaries and allows for an event to be stored into memory potentially via interactions between the cortex and the hippocampus. However, to understand how segmentation contributes to the integration of an episode into long-term memory, as well as to make predictions about the neural mechanisms involved, it is important to first understand the role of the hippocampus-neocortex complex in forming a memory trace. Equally significant is understanding how this trace evolves with time and can be subsequently reactivated.

1.4 The transformative nature of episodic memory

1.4.1 The creation of a memory trace

The hippocampus has specific physiological properties that enable it to quickly transform novel experiences into memory traces. One key factor is its high synaptic plasticity, which allows for efficient and rapid changes in the strength of connections between neurons (Fuchsberger and Paulsen 2022). Furthermore, the hippocampus possesses anatomical connections with multiple neocortical regions, facilitating efficient information exchange between the hippocampus and various areas of the neocortex (Buzsáki 1996; Figure 1.4).

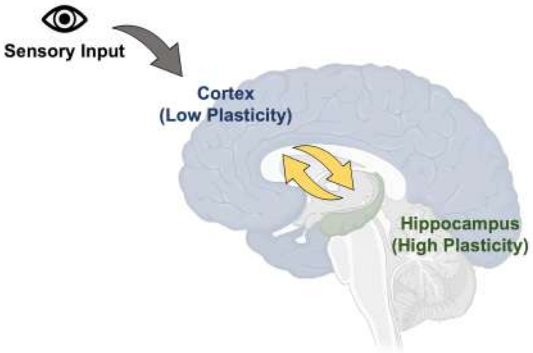


Figure 1.4: The cortex (Blue) receives sensory input which is processed in its sensory regions and sent to the hippocampus (Green) who use that information to create an initial memory trace who is then sent back to the cortex to be stored.

In 1986, Teyler and DiScenna formulated a theoretical perspective, known as the Hippocampus Indexing Theory Teyler and DiScenna 1986, aiming to elucidate the mechanisms underlying the storage and retrieval of information in the hippocampus. According to this theory, the constituent features comprising a specific event trigger patterns of neocortical activity, which are subsequently projected to the hippocampus, leading to the reinforcement of synaptic connections between these regions. As a result, the memory trace corresponds to the concurrent patterns of activity from the neocortex that are represented in the hippocampus.

However, how the hippocampus and neocortical structures interaction evolves across a lifetime of a memory and whether the hippocampus is required for the retrieval of a remote episodic memory it is still a matter of debate. The Standard Model of Systems Consolidation (SMSC: Squire and Alvarez 1995) first proposed that the hippocampus is critical in early encoding stages as the cortex is itself unable to initially support the memory trace creation. With time the hippocampus teaches the memory trace to the cortex so that, after consolidation, the hippocampus is no longer needed to retrieve that particular trace. Its contemporary competing theory is the Multiple Trace Theory (MTT; Nadel and Moscovitch 1997) which proposes that the hippocampus is always involved in the storage and retrieval of any episodic memory, independent of their age. More recently an alternative theory that combines elements from both SMSC and MTT has been proposed and explores what happens to a memory trace when it is reactivated.

1.4.2 Memory transformation through neural reactivation

The Competitive Trace Theory (CTT, Yassa and Reagh 2013) suggests that, when a memory is reactivated, the hippocampus not only recombines the elements of the original trace but potentially adds or subtracts individual contextual features resulting in a new memory trace, weakening irrelevant contextual details and semanticizing that episode. Two distinct phenomena can then result from this process: consolidation or decontextualization. This process could then explain why in the absence of the hippocampus, such like in amnesia cases, patients are still able to retrieve a highly semanticized representation of an event, most likely from the trace stored in the neocortex, which features a core set of important facts but no contextual depth (Hirano and Noguchi 1998; Nadel et al. 2000; Cipolotti et al. 2001). The idea that the hippocampus can transform an episodic memory representation also comes from two mechanistic hippocampal properties: pattern separation and pattern completion. During the rapid encoding of unique experiences, the hippocampus can either reinstate a particular memory trace from only a partial input (*i.e.*, pattern completion; Rolls 2007) or distinguish between overlapping patterns so that a new memory trace can be formed (*i.e.*, pattern separation; Marr 1971; McClelland, McNaughton, and O'Reilly 1995).

What the previous theories (*i.e.*, SMSC and MTT) had in common, and what CTT specially stresses out, is that the consequence of reactivating existing memory traces, both during encoding or driven by new events, is essentially to transform an experience into a long-term memory representation. Neural reactivation plays then a fundamental role in stabilizing newly formed synaptic connections so that they can resist future interference (Figure 1.5). Given its importance, many neuroscientists have spent the past years trying to explain the neural mechanisms involved in this process.

1.4.3 Memory reactivation during sleep and awake behavior

The sequential activation of place cells and its later reactivation during sleep were the first evidence of hippocampal neural reactivation (Pavlides and Winson 1989). Place cells are a type of hippocampal neurons which become active in specific locations or "places" within an animal's environment. When an animal is in a particular location, these place cells fire action potentials, creating a distinctive pattern of firing activity (O'Keefe and Dostrovsky 1971). During periods of rest or sleep, these

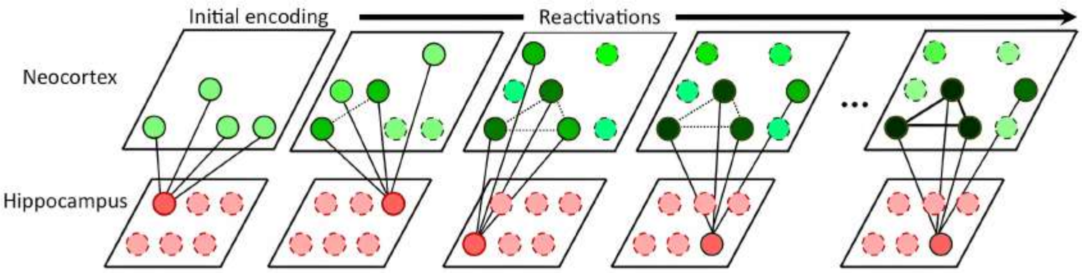


Figure 1.5: Schematic of Hippocampal CTT. Each time a memory is recalled, the hippocampus creates a partially overlapping trace, which competes with similar traces from other recollections in the neocortex. In the hippocampus, the traces are non-overlapping, thanks to pattern separation. However, in the neocortex, the overlapping features become stronger (*i.e.*, consolidated) while the non-overlapping features lose their context. When a memory is recently recalled, an intact hippocampus can help re-contextualize the memory by creating an additional trace. As remote memories are reactivated, the hippocampus still plays a role in recontextualizing the memory. However, the memory itself has already been extensively reinforced through multiple prior reactivations, leading to a well-established and consolidated memory. Adapted from Yassa and Reagh 2013.

same place cells exhibit coordinated reactivation, where the neural firing patterns representing the animal's previous trajectory are replayed in a compressed or accelerated manner, an effect which was labelled for the first time as 'replay' (Nádasdy et al. 1999; Lee and Wilson 2002; Ji and Wilson 2007; Peigneux et al. 2004).

Later work also revealed that replay was not limited to awake 'offline' periods and that it could also occur while animals were awake and engaged in active behavior (Foster and Wilson 2006). Particularly, they found evidence for a reverse replay in which specific episodes of recent spatial activity were replayed in a temporally reversed order (Figure 1.6). They argue that replaying the events in a reversed way allows the immediately preceding events to be evaluated in precise temporal relation to the current reference event, which might be crucial while encoding real life continuous experiences. Reverse replay as also been shown to more frequently represent novel as opposed to familiar environments suggesting a crucial role in rapid learning and consolidation of behaviorally relevant memories (Foster and Wilson 2006). This rapid processing of information is ensured by the fact that replay occurs in a time-compressed manner, with the firing patterns corresponding to the memory trace persisting for shorter durations during reinstatement (O'Neill et al. 2010; Ji and Wilson 2007). The fact that replay occurs also during awake behavior suggests that it might play a role in guiding decisions, planning goal directed trajectories and simulating outcomes from different choices. This view became more evident after Diba and Buzsáki 2007 observations that, during track running, rats' movement initiations was preceded by a forward replay (Figure 1.6). This forward replay has been shown to depict routes ahead of the animal suggesting a role in planning forthcoming actions (Singer et al. 2013). All this evidence show that replay can be used adaptatively according to task demands to either consolidate the just encoded experience or plan future actions.

In humans, due to the difficulty of acquiring single unit electrophysiology data, the evidence for hippocampal replay has been relatively sparse. With the advance of brain recording methods and methodological approaches, replay has now been shown to be present during sleep consolidation, where pattern classification methods were used to compare pattern specific stimuli presented during

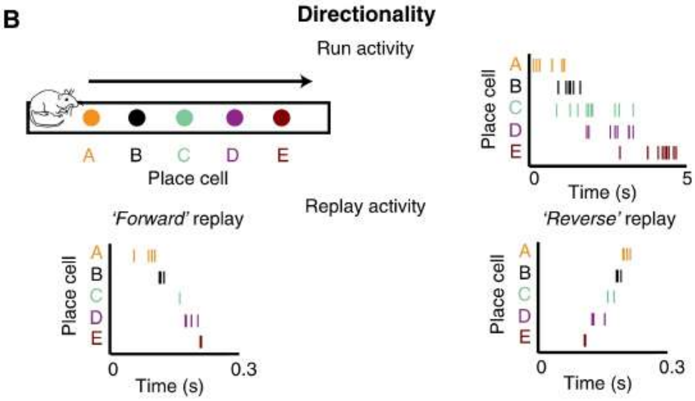


Figure 1.6: During spatial navigation, place cells in the brain activate in a sequential manner to represent the current location of the rodent. Once the rodent completes its journey, these sequential patterns of neuronal activity can be later reactivated in reverse/forward order during periods of rest or at a decision point. This reactivation occurs in a condensed timeframe and plays a functional role in strengthening the learned experience, specifically the memory of the navigated trajectory, over the long term. Adapted from Ólafsdóttir, Bush, and Barry 2018.

encoding to the neural pattern activations elicited during sleep (Schönauer et al. 2017; Schreiner et al. 2021; Sterpenich et al. 2021). Similarly, neural reactivation has been shown to occur in awake periods by comparing the patterns elicited during learning with a post-learning period (Peigneux et al. 2004; Tambini, Ketz, and Davachi 2010; Staresina et al. 2013).

It is then crucial to gain a comprehensive understanding of the neurophysiological signatures involved in the formation and replay of a memory trace. By unraveling the intricate neural dynamics underlying these processes, we can shed light on how memories are formed and ultimately influence behavior. One prominent phenomenon that has garnered considerable attention is sharp-wave ripple (SWR) activity.

1.4.4 The role of Sharp Wave Ripples in memory formation

Sharp Waves are large amplitude, negative polarity activity deflections lasting between 40-100 ms, occurring in the CA1 portion of the hippocampus. In rodents, they are frequently, but not invariably, associated with short-lived fast oscillatory patterns of local field potentials (LFP) in the CA1, known as ripples (150-250Hz) (O'Keefe and Nadel 1978; Buzsáki, Lai-Wo S., and Vanderwolf 1983). The combination of sharp waves and ripples forms the Sharp Wave Ripple Complex, known as the most synchronous event in the brain, and capable of enhancing transient excitability in the hippocampus and its partner structures (Buzsáki 1986; Chrobak and Buzsaki 1994). Neurons involved in SWR events are sequentially organized in an orderly structure that reflect a temporally compressed version of the sequential neuronal firing patterns of the waking animal (Nádasdy et al. 1999; Lee and Wilson 2002). This organized activity suggests that SWRs neuronal activity may play a critical role in memory consolidation by facilitating the transfer of information from the hippocampus to other brain regions, such as the neocortex, for long-term storage, in line with the previously mentioned consolidation models (Buzsáki 1986). During a SWR, the neurons in the hippocampus fire in a synchronized manner, causing a brief but intense burst of activity that helps to strengthen the connections between neurons that were activated during waking experiences (Buzsáki 1986; Buzsaki et al. 1992; Bragin et al. 1999).

Studies demonstrated the importance of SWRs for memory-dependent behaviors by manipulating or disturbing their occurrence during sleep, providing the first evidence for their role in memory consolidation. One of the first studies in rats investigated neuron firing during non-REM sleep episodes, separated by exploratory activity in a new environment. Neurons most active during waking, even if infrequent during pre-exploration sleep, showed the strongest association with SWRs in the second sleep episode (Buzsáki 1986). When SWRs get interrupted during hour-long periods of sleep, or rest following an experience, a decrease in the speed of learning in hippocampal-dependent spatial memory tasks occurs (Ego-Stengel and Wilson 2010).

While SWRs are primarily associated with sleep and memory consolidation, studies have also suggested their importance in awake behavior. Research has demonstrated that they can occur during awake states, particularly during periods of rest and quiet wakefulness, and may play a role in information processing and consolidation even in the absence of sleep. They have been shown to be associated with both reverse (Foster and Wilson 2006) and forward replay (Diba and Buzsáki 2007) and their interruption to impair performance in a spatial alternation working memory task, indicating that awake ripples also play a role in navigational decision making (Jadhav et al. 2012) (Figure 1.7).

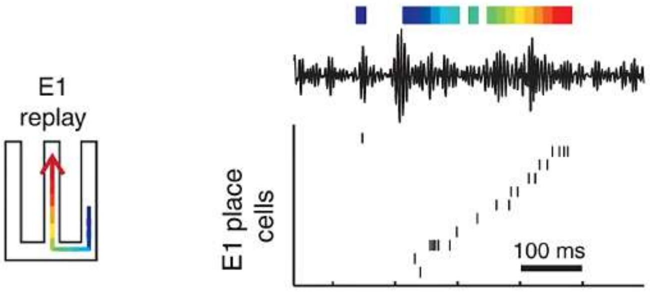


Figure 1.7: Raster of place cells that were activated during the SWRs identified in the filtered local field potential (LFP) shown above. The color bar shows the colors associated with each of the trajectory locations seen on the left. Place cells are activated during SWR and result in the reactivation of the locations the animal took during exploration. Adapted from Karlsson and Frank 2009.

Another potential role of SWR is in the support of plasticity and communication between the hippocampus and cortical regions. In rodents, electrical stimulation after SWRs during sleep was shown to enhance coordinated activity between the medial Prefrontal Cortex (mPFC) and hippocampus, improving memory for briefly presented objects in context (Maingret et al. 2016). This study provided the first tangible evidence of the coordination and involvement of SWRs in communication within the cortico-hippocampal circuit and its role in memory consolidation. Since then, these transient events have also been shown to accompany widespread cortical and subcortical activations (Karimi Abadchi et al. 2020; Gomperts, Kloosterman, and Wilson 2015).

In humans, they are believed to reflect coordinated activity between the hippocampus and neocortex, allowing for the efficient transfer of information from short to long-term memory (Todorova and Zugaro 2020; Vaz et al. 2019; Norman et al. 2021; Dickey et al. 2022), and have recently been show to support the formation and retrieval of associative memories (Kunz et al. 2022; Sakon and Kahana 2022).

In conclusion, accumulating evidence suggests that SWRs play a crucial role in the replay of prior experiences and serve as essential mechanism for information transfer from the hippocampus to other brain regions, facilitating long-term storage of memories. Moreover, recent research indicates that SWR-mediated replay may extend beyond memory processes, influencing decision-making and planning.

1.4.5 Replay as a mechanism for planning

Spatial navigation and planning involve not only recollection of past experiences but also the consideration of alternative scenarios and the determination of optimal choices. Indeed, the evidence for the existence of forward replay during SWRs, is suggestive of the role of replay for exploring potential routes or extracting goal-directed vectors as it allows for the depiction of routes ahead of the animal (Diba and Buzsáki 2007; Singer et al. 2013). However, the precise mechanisms by which the brain dynamically switches between replaying past experiences to support memory consolidation or projecting future actions remain an intriguing question.

One hypothesis is that it does so according to task demands, so that hippocampal replay may be enhanced when planning is beneficial. In a recent magnetoencephalography (MEG) study by Wimmer et al. 2023, where participants were asked to navigate two separate and independent environments with different start states but converging shared paths, so that retaining a memory of an "unattended" environment was required while learning within the "attended" one, researchers show that during decision-making moments, replay strength was related to the relative benefit of goal-directed control of behavior. By contrast, after reward feedback, replay of alternative environment paths was related to recent experience of the unattended environment, demonstrating then the distinct roles of replay in memory and decision-making, within a single task (Wimmer et al. 2023).

Each of the aforementioned studies offer empirical evidence to suggest that hippocampal replay not only play a role in memory consolidation and retrieval of past experiences, but also in the planning of future actions. The presence of generated sequences within the hippocampus offers a physiological mechanism for the replay of past events so that one can form speculative scenarios involving alternative actions and their potential consequences, without the need for actual testing or execution. The identification of replay's influence on various cognitive processes, including navigational behavior (Pfeiffer and Foster 2013), learning (Ego-Stengel and Wilson 2010), and working memory (Jadhav et al. 2012), offers compelling evidence for the involvement of the hippocampus beyond its conventional role in memory storage and consolidation. These findings have, for the most recent years, sparked discussions regarding the hippocampus' integrative function and general role in the creation of mental representations of our experiences, which will be discussed in the upcoming section.

1.5 Creating relational map representations

Successful planning requires not only accessing memories for previous events but also integrating these same memories to make predictions about action consequences. The hippocampus has this double capacity. First it encodes the relations between different features of an experience and, when elements of a current experience overlap with those of a previously encoded one, integrate the new memory with an old one (Lisman et al. 2017). Once this ‘relational map’ is formed, elements within the map that were never directly experienced together can be inferred, allowing for generalization in novel situations (Momennejad et al. 2018; Garvert, Dolan, and Behrens 2017; Schapiro et al. 2016; Brown and Green 2016).

Indeed, animals efficiently extract abstract relationships between landmarks, events, and other types of conceptual information, often from limited experience. In physical space, hippocampal place cells and grid cells become active when an animal occupies a specific location in an environment (O’Keefe and Nadel 1978) and its arranged firing fields provide a spatial coordinate system that helps to establish relationships between different places (Bush et al. 2015). In non-physical dimensions, the human hippocampus was also shown to extract the proximity along other dimensions such as time, so that events occurring closer together in time elicit similar neural patterns (Ezzyat and Davachi 2014). The construction of relational maps has also been extensively studied through the use of modular networks, wherein stimuli or states are conceptualized as nodes in a graph with edges or connections representing possible transitions between them. These provide a unique and ecologically valid framework, as they closely resemble real-world scenarios where information is organized into distinct functional units or events (Karuza, Thompson-Schill, and Bassett 2016). Research in statistical learning has revealed that modules, which are communities of densely connected nodes within transition networks, can be observed in brain imaging data (Schapiro et al. 2016) and that the hippocampus is particularly involved in learning the structure in these community-based sequences (Schapiro et al. 2016). This line of research has led to a growing understanding that the way individuals perceive and represent a transition structure is heavily influenced by its higher-order organization and how different units are connected. While these accounts have provided support for the principles of predictive coding in the context of lower-level abstract processing, it remains uncertain whether and how similar mechanisms are at play when we consider the individual episodes or events that we personally experience. How do people segment such continuous streams of information, identifying where one event starts and another begins?

1.5.1 Organizing the world into different event representations

In daily life, we continuously draw on past experiences to predict the future. When these predictions are incorrect, we must update our internal models of the world to support adaptive behavior. If faced with a new experience, a previously similarly experienced memory trace can be retrieved through associative reactivation of the neocortical-MTL representations encoded in that trace (Yassa and Reagh 2013). If any difference between past and present experience happens to violate the expectations set by our episodic memory, then an error in prediction is signaled and a new memory trace is created for that new experience (Sinclair et al. 2021). Indeed, prediction error or surprise have a central role in most accounts of event parsing so that event boundaries are identified based on non-uniform transition probabilities (Reynolds, Zacks, and Braver 2007). Within an event, a given observation is highly predictable from preceding ones, whereas the observation beginning a new event is less predictable. This means that uncertainty about an upcoming observation or surprise at the occurrence of an unpredicted observation, can provide a cue for event segmentation and provide the mechanism through which the brain organizes the world into different event representations.

The EST proposed by Zacks et al. 2007 stated that at points when activity becomes less predictable transient increases in prediction error would be detected and the event model would be updated (Figure 1.8). To assess this, in a later study they asked participants to watch a series of movie clips depicting everyday activities (Swallow, Zacks, and Abrams 2011). At times, the clip was paused, and participants were asked to predict what would occur in the next 5 seconds. When an intervening event boundary was present, as determined by independent observers, prediction accuracy decreased, and the substantia nigra, a region associated with dopaminergic responses to reward prediction errors, exhibited greater activation. Concurrently, a neural network model incorporating perceptual prediction error as a gating signal to update event representations successfully identified simulated event boundaries solely based on prediction error transitions (Reynolds, Zacks, and Braver 2007).

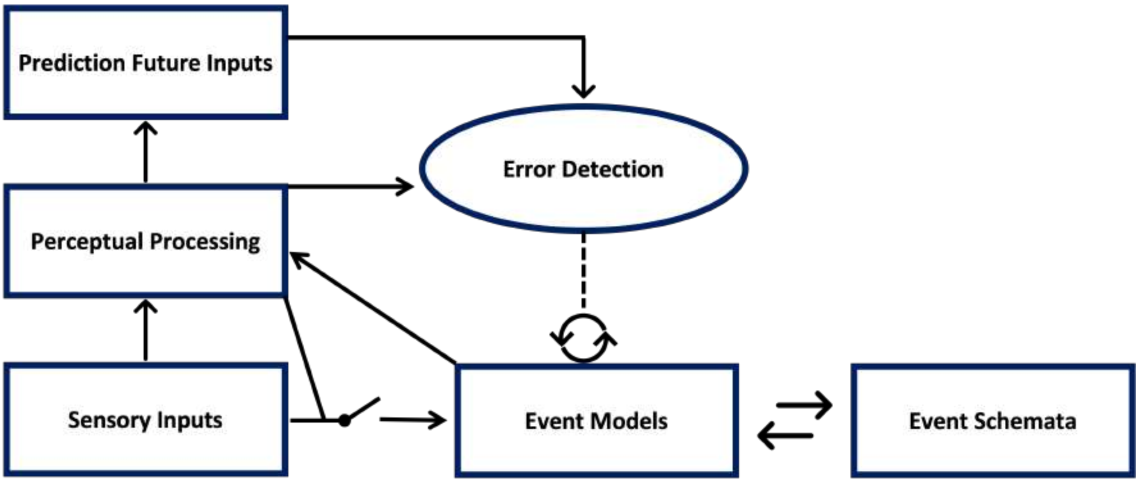


Figure 1.8: Schematic representation of the EST model. The entrance of information from sensory inputs to event models is done through a gated mechanism in which when a mismatch between predicted inputs and actual sensory input occurs, a prediction error is generated which results in the reset of the current event model. Adapted from Zacks et al. 2007.

However, prediction errors might not always be necessary to create an event boundary. For instance, in the context of narrative reading where an event shift is hinted at in advance, readers continue to exhibit slower response times when probed about their memory of the pre-shift events, even though they no longer experience surprise or a deceleration in their reading pace (Pettijohn and Radvansky 2016). This intriguing finding suggests that even when a change is expected, if it holds sufficient meaning, it can still prompt event segmentation in memory. In another study, Schapiro et al. 2013 found that people could identify boundaries in a series of stimuli based only on their learned temporal transition statistics. For that they applied a clever graph manipulation in which every single node was connected to four neighboring nodes so that every transition that occurred was equally likely. That meant that transitioning between communities (*i.e.*, an abstraction of an event boundary) would never give rise to moments of relative uncertainty or surprise as it was probabilistically equally likely to a within community transition (Figure 1.9). Nonetheless, they found that people could still identify boundaries solely based on their learned temporal transition statistics. Notably, building more accurate mental representations of a network allows humans to better anticipate future items and events (Schapiro et al. 2013; Karuza, Thompson-Schill, and Bassett 2016; Karuza et al. 2017; Kahn et al. 2018; Lynn and Bassett 2020), which is a guiding principle for optimal decision-making in complex environments.

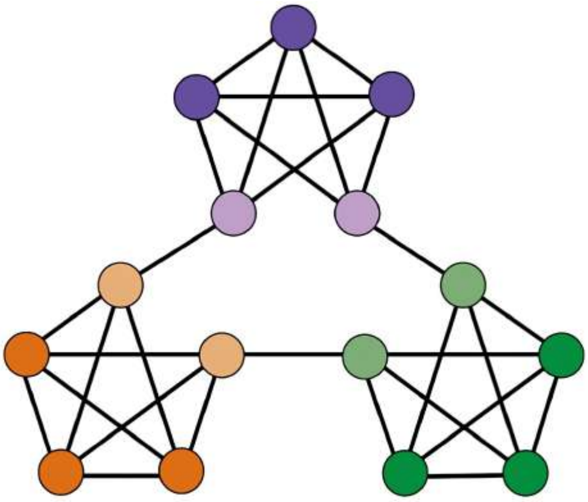


Figure 1.9: Each community corresponds to an abstract representation of an event and each edge node is associated with a possible transition between events such as an event boundary. Adapted from Schapiro et al. 2013.

Authors have made compelling arguments demonstrating that humans possess an implicit ability to generate event boundaries based on various factors. These factors include the distinct temporal associations between consecutive stimuli (Schapiro et al. 2013), changes in the causal structure of the environment (Kurby and Zacks 2008; Radvansky 2012), and shifts in our goals (DuBrow and Davachi 2016). These studies have highlighted the significance of these factors in influencing the segmentation of continuous experiences into distinct events. Importantly, these segmentation processes seem to be driven by mechanisms related to both memory and decision-making.

While significant progress has been made in understanding the factors that contribute to event segmentation, numerous questions remain unanswered. The precise mechanisms by which individuals learn and represent these transitions are still not fully understood. Therefore, investigating the neural underpinnings and cognitive processes involved in the creation of an event boundary is of utmost importance and remains a crucial question in this field.

1.6 Boundaries: how do we wrap up an event?

Event boundaries then play a critical role in episodic memory by facilitating the segmentation of continuous experiences into discrete episodes, aiding in memory organization and retrieval. When an event boundary occurs, it serves as a natural break in the stream of experiences, allowing for the encoding and storage of the preceding event as a distinct episode. Research by Radvansky, Krawietz, and Tamplin 2011 demonstrated that event boundaries can lead to improved recall and recognition of contextual information. They found that participants showed better memory performance for information within an event compared to information that spanned across multiple events. These findings suggest that event boundaries contribute to the formation of coherent and separate memory representations.

Event boundaries may also provide natural breakpoints for evaluation and anticipation. As individuals approach an event boundary, their cognitive systems generate expectations about what might occur next (Kurby and Zacks 2011). These predictions guide attentional processes and influence decision making by shaping the evaluation of options and potential outcomes. According to the findings of Bornstein and Norman 2017, when individuals are reminded of an image they encountered in a previous event, their decision-making process is not solely influenced by the specific experience associated with that image. Rather, their decisions are biased by the overall summary of their experiences during that entire event, with decisions being biased by incidental memory probes that reminded participants of past choices within that event. This discovery suggests that event segmentation plays a crucial role in facilitating the interaction between episodic memory and decision making.

However, several intriguing questions remain regarding the mechanisms behind the detection and segmentation of events. To unravel these mechanisms, it is crucial to investigate the cognitive processes and cues that enable individuals to recognize and differentiate between events. What are the specific cognitive operations and neural processes that allow us to perceive and demarcate event boundaries? Understanding these processes would provide valuable insights into how the brain parses continuous experiences into discrete events. Moreover, exploring the impact of event boundaries on memory formation and the integration of information across events is an important avenue of research. How do event boundaries influence the consolidation of memories? Examining this question would enhance our understanding of the factors that shape memory consolidation and the formation of coherent memory representations.

Addressing these questions holds the potential to deepen our understanding of the mechanisms underlying the role of event boundaries in episodic memory. By exploring the neural substrates, cognitive processes, and behavioral consequences associated with event segmentation, we can gain valuable insights into the fundamental principles that govern human cognition. Additionally, these findings could have practical applications, informing fields such as education, communication, and user experience design, where effective organization and presentation of information rely on an understanding of event structure and its impact on memory and decision making.

Chapter 2

Research Aims

Events in real-world experiences are often complex and dynamically unfolding. Understanding how event boundaries operate in dynamic and continuous experience is an ongoing research challenge and so exploring event segmentation in ecologically valid and naturalistic settings can provide insights into the nature of event processing. Within my doctoral project, my aim is to test that boundaries serve as pivotal moments in time when the brain orchestrates the conversion of external inputs into an internal representation of our experiences. This intricate process would involve a cascade of cognitive mechanisms encompassing memory encoding and replay, as well as learning and decision making. By delving into these interconnected processes, I seek to provide evidence and substantiate the role of boundaries in shaping our cognitive framework.

Next, I will argument each specific aim in more detail:

- **Aim 1: Assess if just-experienced episodic information is replayed at event boundaries in a context of a naturalistic task (Study 1)**

The EST refers to boundaries as spikes in prediction error that affect not only our perception of the just experienced information but also our expectations to what might happen in the immediate future. These predictions are essential for long-term organization, such that elements within event can be bound together cohesively. Thus, event boundaries are strong candidates as mediators of memory consolidation during naturalistic experience. The first prove of this link was found by Ben-Yakov and Dudai 2011. Their research showed that brain-activity, acquired with fMRI, time-locked to the offset of narrative episodes occurring in a set of regions including the hippocampus, was correlated with subsequent memory performance. The hippocampus is known to play an important role in episodic memory formation so, the fact that its activity is triggered by activity at event boundaries (Baldassano et al. 2017; Ben-Yakov and Henson 2018; Ben-Yakov and Dudai 2011;Ben-Yakov, Eshel, and Dudai 2013), proposes that some memory consolidation of just encoded events occurs at the boundary level which leads to the registration of the event into long-term memory. In a later study, using pattern similarity analysis, Sols et al. 2017 showed the first evidence that just-experienced episodic information may be replayed at boundaries. Given so, in this first study our main goal was to further explore the hypothesis that online encoding of a continuous stream of information occurs at the offset of each event, moments after a boundary is perceived. We hypothesized that the brain activity time-locked to a boundary could be predictive of later reinstatement of that specific event which would generalize previous findings (Sols et al. 2017) to a naturalistic encoding setting.

- **Aim 2: Assess the role of ripples in the encoding of events and its impact in event segmentation (Study 2)**

The communication between the hippocampus and neocortex is crucial for the encoding of events and the formation of long-term memories. The transfer of memories from the hippocampus to the neocortex is facilitated by coordinated neural activity, including ripples. These transient events have been extensively studied in rats and shown to accompany widespread cortical and subcortical activations (Karimi Abadchi et al. 2020; Gomperts, Kloosterman, and Wilson 2015). They are believed to reflect coordinated activity between the hippocampus and neocortex, allowing for the efficient transfer of information from short to long-term memory (Todorova and Zugaro 2020; Vaz et al. 2019; Norman et al. 2021; Dickey et al. 2022).

The presence of ripples in humans has recently been proven (Axmacher, Elger, and Fell 2008) and associated to memory processes (Vaz et al. 2020; Vaz et al. 2019; Norman et al. 2019; Kunz et al. 2022; Sakon and Kahana 2022) but never shown to be associated with event boundaries during the encoding or recall of real-life experiences or to modulate the communication between hippocampus and neocortex in naturalistic encoding. Our hypothesis is that the process of memory consolidation at event boundaries is mediated by bursts of ripple activity in the hippocampus. Additionally, we hypothesize that throughout an event there is a coupling of ripples between the hippocampus and cortical areas (Vaz et al. 2019; Kunz et al. 2022) which reflects a possible integration of memory details for the corresponding event and facilitates later recollection of that event.

- **Aim 3: Assess if boundaries help organize space into a hierarchical map representation and aid in goal-directed behavior (Study 3)**

The hippocampus has emerged as a key player in the prospective encoding of future events, as previous research has indicated (Addis, Wong, and Schacter 2007; Pfeiffer and Foster 2013). It is evident that our ability to learn from past experiences is critical for optimizing future decision-making. Given that event boundaries represent moments when a prediction error mechanism is updated (DuBrow et al. 2017; Gershman, Markman, and Otto 2014; Zacks et al. 2007), it is reasonable to propose that these moments may have a significant role in determining appropriate future actions.

Decision-making processes in complex environments are enhanced by the rapid access of a structured representation of the underlying relationships between elements, and so we hypothesized that rapidly tracking boundary items may foster better performance in a modular network, allowing for the construction of a mental representation of the hierarchical structure of the map which would be necessary for enhancing goal-directed behavior.

Chapter 3

Study 1: Rapid Memory Reactivation at Movie Event Boundaries Promotes Episodic Encoding

3.1 Summary

Segmentation of continuous experience into discrete events is driven by rapid fluctuations in encoding stability at context shifts (*i.e.*, event boundaries), yet the mechanisms underlying the online formation of event memories are poorly understood. We investigated the neural per-time point spatial similarity patterns of the scalp EEG activity of 30 human participants (male and female) watching a 50 min movie and found that event boundaries triggered the rapid reinstatement of the just-encoded movie event EEG patterns. We also found that the onset of memory reinstatement at boundary onset was accompanied by a left-lateralized anterior negative event-related potential (ERP) effect, which likely reflects the detection of a shift in the narrative structure of the movie. A data-driven approach based on Hidden Markov modeling allowed us to detect event boundaries as shifts between stable patterns of brain EEG activity during encoding, and to identify their reactivation during a free recall task. These results provide the first neurophysiological underpinnings for how the memory systems segment a continuous long stream of experience into episodic events.

3.2 Introduction

Memory systems transform the stream of our continuous experience into a sequence of episodic memory units to be recalled in the future. While extensive research has been conducted to understand how the brain supports the formation of discrete, brief novel information, it is only recently that psychologists and neuroscientists have started exploring the mechanisms that account for episodic memory formation during a continuous stream of experience. A widely accepted view is that we naturally segment continuous experience into events, and that event boundaries are driven by moments in time when prediction of the immediate future fails (Zacks et al. 2007) or by fluctuations in contextual stability (Clewett and Davachi 2017). Segmentation affects not only our perception of the experience, but its subsequent organization in long-term memory (Kurby and Zacks 2008; Radvansky 2012; Sargent et al. 2013), such that elements within an event are bound together more cohesively than elements across events (Ezzyat and Davachi 2011; DuBrow and Davachi 2013; DuBrow and Davachi 2014; Horner et al. 2016). Human neuroimaging studies using naturalistic video clips have set important findings that align well with these behavioral findings. They have shown that a distributed network of brain regions comprising the hippocampus and neocortex are involved during event segmentation and that their dynamics during encoding provide a basis for how we parse the temporally evolving environment into meaningful units. They revealed that the brain organizes the ongoing input into episodic events by detecting changes in the stability of activity patterns. Stable patterns of activity at higher-level brain regions during encoding are thought to maintain a stable event representation despite fluctuations in the ongoing sensory input (Baldassano et al. 2017; Chen et al. 2017). Shifts in stability that coincide with perceived boundaries induce a neural response at the hippocampus (Ben-Yakov and Dudai 2011;Ben-Yakov, Eshel, and Dudai 2013; Ben-Yakov and Henson 2018; for similar findings in rodents, seeBulkin et al. 2020) and the degree to which hippocampal activity at boundaries couples with cortical patterns of activity predicts pattern reinstatement during later free recall Baldassano et al. 2017) thereby indicating that the hippocampus may be responsible for binding cortical representations into a memory trace online during encoding (McClelland, McNaughton, and O'Reilly 1995; Norman and O'Reilly 2003; Moscovitch et al. 2005). However, an important question remains unanswered: which neural mechanisms support the binding of the encoded information of an event upon boundary detection? And more importantly, how can we investigate these neural mechanisms in ecologically valid circumstances that can inform us about their nature in real life environments? To address this issue, we recorded scalp brain EEG while 30 participants watched a single 50 min movie clip and asked whether time-resolved fluctuations in neural similarity elicited during movie viewing reflected event segmentation. Leveraging the fine-grained temporal resolution of the EEG signal, we then tested the hypothesis that moments in time after perceived, event boundaries during movie viewing would exhibit reactivation of the just-encoded episode, and that this reactivation would promote consolidation of the encoded event into long-term memory. Indeed, the reactivation of encoded episodes upon boundary detection would be in line with animal research using EEG recordings showing that memory replay of the just-encoded event promoted its memory formation and consolidation (Carr, Jadhav, and Frank 2011) and with recent EEG research in humans that showed that memory reactivation at picture boundaries during sequence encoding promoted a linked memory representation across events (Sols et al. 2017). The extent to which boundary-triggered memory reactivation impacted memory formation during movie viewing would offer valuable insights into how the brain shapes the unfolding experience into memory under ecologically valid situations.

3.3 Materials and Methods

3.3.1 Participant sample

Thirty-three Spanish speakers (30 right-handed, 20 females, age range 18 – 46 years, mean=22 years) participated for pay (10€/h). Participants were recruited from the University of Barcelona and the broader community. All participants were healthy and did not consume psychoactive substances. Informed consent was obtained from participants in accordance with procedures approved by the Ethics Committee of the University of Barcelona. Data from 2 participants were discarded due to falling asleep during the experiment, and 1 due to too much muscular artifact in the data. Thus, the final sample of participants included in the study was 30.

3.3.2 Experimental Design

Our primary dataset consisted of 30 participants who watched the first 50 min of the first episode of *BBC's Sherlock*, a stimulus already used by Chen et al. 2017 and Baldassano et al. 2017, dubbed in Spanish. They were then asked to freely recall the episode without cues while being recorded using an audio recorder. The audio files were later analyzed to access participants' length and richness of the recall, with total recall times ranging from 6 to 44 min (and a mean of 15 min). At the beginning of the movie, a 30 s audiovisual clip ("Let's All Go to the Lobby") was presented to set participants' attention. The experimental design was implemented on ePrime 2.0 (Psychology Software Tools).

3.3.3 EEG recording and preprocessing

EEG was recorded using a 32-channel system at a sampling rate of 500 Hz, using a BrainAmp amplifier and tin electrodes mounted in an electrocap (Electro-Cap International) located at 29 standard positions (Fp1/2, Fz, F7/8, F3/4, Fc1/2, Fc5/6, Cz, C3/4, T3/4, Cp1/2, Cp5/6, Pz, P3/4, T5/6, PO1/2, O1/2) and at the left and right mastoids. An electrode placed at the lateral outer canthus of the right eye served as an online reference. EEG was rereferenced offline to the right and left mastoids. Vertical eye movements were monitored with an electrode at the infraorbital ridge of the right eye, and an independent component analysis was run on MATLAB's EEGLAB toolbox (Delorme and Makeig 2004) to correct for eye movements and remove extremely noisy components (no more than 6 components were removed). A low pass filter of 20 Hz was applied to reduce the presence of muscular artifacts (Pérez, Carreiras, and Duñabeitia 2017). The data were then normalized before every analysis by z scoring all time points so that the mean of every electrode is 0 across time.

3.3.4 Event boundary annotations by human observers

Six external participants, who did not take part in the electrophysiological recording session of the study, were asked to watch the movie. Using the standard event segmentation approach (Newtson 1973; Zacks et al. 2010; also used in Baldassano et al. 2017; Chen et al. 2017; Ben-Yakov and Henson 2018), participants were requested to annotate with precision the temporal point at which they felt "a new scene is starting; these are points in the movie when there is a major change in topic, location or time." Participants were also informed that each event should be between 10 s and 3 min long, and we asked them to write down a short title for the event. With the participants' boundary annotations, we looked for those boundary time points that were consistent across observers. To find a statistical threshold of how many observers should coincide in a given time point to be different from chance in our data, we shuffled the number of observations 1000 times and created a null distribution of the resulting coincident time points. An $\alpha = 0.05$ as a cutoff for significance indicated that boundary time points at which at least 3 observers coincided in (considering 3 s as possible window of coincidence as in Baldassano et al. 2017) could not be explained by chance. This approach resulted in a model composed by 38 events (minimum = 4 s, maximum = 444 s, and mean = 76.02 s). The model was compared with the one obtained in Baldassano et al. 2017. To do so, the distances between the boundaries in this and the previous study were calculated. A null distribution was then created by shuffling in time the previous study boundaries while maintaining the length of the events, and the distances between the boundaries in the current study and the new shuffled ones were computed. The average real distances were then compared with the null distribution to compute a z value, which was converted to a p value. This analysis resulted in a p = 0.12, which indicates that the human annotation boundaries used in the current study are not statistically different from the ones used in the previous study with another sample of participants.

3.3.5 Verbal Recall Analysis

After 15 min of rest, all 30 participants who participated in the EEG encoding session were asked to retell the story they had just watched, without any cues or stimulus. EEG was also collected during this time, and verbal recall was recorded through an audio recorder for later analysis. The audio files recorded during the free verbal recall were analyzed by a laboratory member who was a native Spanish speaker, using the list of events from the human annotations model. An event was counted as recalled if the participant described any part of the event and were counted as out of order if they were initially skipped and later described in the narrative or if an event was recalled earlier than it should. However, the latter case rarely happened (on average, $< 0.1\%$).

3.3.6 Finding event structure in the EEG data

To validate the event segmentation model extracted from human annotations on the EEG data collected from the primary sample in the study, we generated, for each of the individuals, a temporal correlation matrix computed by correlating the 29 electrodes with the same 29 electrodes for each of the time points after downsampling the data by segmenting the EEG into bins of averaged data from 100 sample points (*i.e.*, 200 ms). We chose this interval as a compromise between preserving data structure and reducing computational time in the analyses. Next, we averaged the correlation values within each of the 38 events and ran a permutation test (N = 1000) with null boundaries picked by shuffling the temporal order of the events while maintaining their lengths. The within-event correlation values were compared with the permuted values using an α of 0.05 as a cutoff for significance (see Figure 3.2b).

3.3.7 Shared event neural patterns across individuals during movie viewing

Following previous fMRI findings (Chen et al. 2017), we examined whether neural patterns elicited by events during movie viewing were similar across individuals in our sample. To address this issue, we computed Movie-Movie correlations by comparing movie patterns of each event from one participant with the movie pattern for the same event averaged across the remaining participants. This resulted in an across participants similarity analysis. To assess whether the correlation values were statistically significant, a permutation test (N = 1000) was computed, using an α of 0.05 as a cutoff for significance, by shuffling the event patterns of the hold-out and compare them with the intact order for the remaining participants.

3.3.8 EEG pattern similarity within and across events

A similarity analysis was calculated for EEG neural activity before and after boundaries during movie viewing. The similarity analysis was performed at individual level and included spatial (*i.e.*, scalp voltages from all the 29 electrodes) and the temporal features, which were selected in steps of 20 sample points (40 ms) of the resulting z-transformed EEG single trials. The similarity analysis was calculated using Pearson correlation coefficients, which are insensitive to the absolute amplitude and variance of the EEG response. The similarity analysis was computed on trial-to-trial EEG segments of 10 s preboundaries and postboundaries identified in the event segmentation model. To ensure that differences between before and after the boundary were not arising just due to intrinsic temporal contiguity properties of the EEG signal, we first split preboundary and postboundary 10 s EEG segments in two equal EEG vectors of 5 s. Thus, preboundary event correlations were performed between the interval -10 s to -5 s and the interval -5 to 0 s before the boundary. Between-event correlations were performed between -5 s to 0 and 0 to 5 s, were 0 corresponded to the boundary. Postboundary event correlations were performed on EEG data from the interval 0 to 5 s and the interval 5 to 10 s after the boundary. Point-to-point correlation values were then calculated, and the resulting single trials 2D correlation matrix was smoothed using a mean filter over a rectangle of 10 sample points (*i.e.*, 400 ms). Smoothed single-trial correlation matrices were then averaged for each individual and condition separately. Differences were statistically compared by means of a repeated-measures ANOVA, including type of event as a 3-level factor (preboundary, between-event, and postboundary). Statistical significance was set at $p < 0.05$. A paired-sample t test was used to test for statistical significance between condition pairs.

An EEG similarity analysis was also performed on 20 s windows of EEG as a function of whether events preceding a boundary were later recalled or forgotten. The 10 s EEG signal included 20 s surrounding a boundary. Similarity analysis was implemented at single-trial level by correlating point-to-point the spatial EEG features surrounding the boundary. As in the previous analysis, single-trial 2D correlation matrices were smoothed using similar parameters before they were averaged. To account for differences between recalled and forgotten conditions, a cluster-based permutation test was used (Maris and Oostenveld 2007), which identifies clusters of significant points in the resulting 2D matrix in a data-driven manner and addresses the multiple-comparison problem by using a nonparametric statistical method based on cluster-level randomization testing to control the family-wise error rate. Statistics were computed for every time point, and the time points whose statistical values were larger than a threshold ($p < 0.05$, two-tail) were selected and clustered into connected sets on the basis of *x,y* adjacency in the 2D matrix. The observed cluster-level statistics were calculated by taking the sum of the statistical values within a cluster. Then, condition labels were permuted 1000 times to simulate the null hypothesis, and the maximum cluster statistic was chosen to construct a distribution of the cluster-level statistics under the null hypothesis. The nonparametric statistical test was obtained by calculating the proportion of randomized test statistics that exceeded the observed cluster-level statistics.

3.3.9 EEG-evoked responses at boundary onset

Event-related potentials (ERPs) at boundary onset were calculated for each individual as a function of whether events were later recalled or forgotten in the free recall task. To obtain the ERPs, we applied a low-pass filter of 12 Hz to the none-downsampled EEG data. Then, epochs of -1000 to 2000 ms were chosen around each of the boundary time points determined from the event segmentation model. The preboundary interval (-100 to 0 ms) was used for baseline correction. ERP differences between recalled and forgotten conditions were investigated starting at 0 to 2000 ms after each boundary onset. Statistical significance of the differences between conditions was assessed by a cluster-based permutation test.

3.3.10 Brain sources of ERPs

Low-resolution tomography analysis (sLORETA) (Pascual-Marqui 2002) was used to reconstruct the source space for ERP differences at boundary onset. This method performs localization inference based on images of standardized current density, which corresponds to the 3D distribution of electric neuronal activity that has maximum similarity (*i.e.*, maximum synchronization), in terms of orientation and strength, between neighboring neuronal populations (represented by adjacent voxels). sLORETA was calculated separately for each participant's averaged ERP triggered by boundaries that followed events that were later recalled and forgotten. Source reconstruction for each condition was compared, and results were displayed by means of t values (paired t test, one-tailed).

3.3.11 Reinstatement of EEG event patterns during free recall

We adapted the Hidden Markov modeling (HMM) approach used in a recent fMRI study by Baldassano et al. 2017 and tested the extent to which it identified EEG-based latent-states during recall according to the event segmentation model constructed through human annotations during movie watching. The model is a variant of an HMM in which the latent variables are the event labels s_t for each time point *t* and the spatial signatures m_k (brain activity patterns across all EEG channels) for each event *k*. From the observed brain activities b_t, we infer both s_t and m_k. The model is set to assume that, for all the participants, the event starts in $s_1 = 1$ and ends with $s_T =$ *K*, where *T* is the total number of time points and *K* is the total number of events. We assume that, in each time point, we can either advance to the next state or remain in the same one, which results in a transition matrix where all elements are zero, except for the diagonal and the adjacent off-diagonal. An isotropic Gaussian model is used to compute the observation model so that the probability that a given observation, b_t, is created by a state $s_t =$ *k* can be given by the following:

$$P(b_t|s_t = k) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-(\frac{1}{2\sigma^2})\|z(b_t - z(m_k))\|_2^2} \tag{3.1}$$

where z() denotes the z-score function. The z-scoring of the brain observations and the mean activity patterns result in a proportionality between the log probability of observing brain state b_t in an event with signature m_k and the Pearson correlation between b_t and m_k plus a constant offset as follows:

$$log(P(b_t|s_t = k)) \propto r(b_t, m_k) \tag{3.2}$$

To ensure that all states are visited, the observation probabilities $P(b_t|s_t = k)$ are modified by setting $P(b_T|s_T = 0)$, for all $k \neq K$ so that, on the final time point, only the final state *K* could have generated the data. To ensure that all possible event segmentations have the same prior probability, a dummy absorbing state *K+1* is created, so that the transition probabilities for state *K* are identical to those for previous states. We set $P(b_t|s_t = K + 1) = 0$ so that this state cannot actually be used. The data were downsampled by segmenting the EEG into bins of averaged data from 100 sample points (*i.e.*, 200 ms) to reduce the computational time in the analyses. We used the mean EEG patterns of each of the events identified by the human annotations model on encoding to model the EEG data during recall. This was accomplished by using the mean patterns from the human annotations events as input on the forward–backward step. For each participant, the HMM was applied to the continuous recall EEG data to obtain a probabilistic assignment of latent event states consistent with the human annotations model obtained during movie watching. The resulting model probabilities $P(b_t|s_t = k)$ were then used to identify the event transition points during recall, as time points when the most likely event changed. We then tested the extent to which human annotation-based EEG patterns elicited during movie watching were similar to those estimated by HMM search during recall. As in the previous analysis, we ran an event-to-event correlation analysis between movie and recall and calculated an averaged correlation measure, as a proxy of the overall degree of similarity over the entire event segmentation model between the two sets of data. To assess statistical significance, we created a null distribution by shuffling the lengths of the human annotation events before running the HMM and computing the correlation between the movie events and the shuffled HMM-identified recall events. This procedure was applied 1000 times, and an α of 0.05 was used as a cutoff. If the forward–backward step correctly identifies events similar to encoding, we expect to find higher correlation values than the ones obtained by trying to identify the same patterns but shuffled in time. In case the correlation values obtained are similar to the ones obtained by using the null distribution, one can infer that the patterns identified by the model were identified just by chance and were just a poor match done by the model.

3.3.12 EOG artifacts as potential confounds

To statistically assess whether the existence of potential eye movement artifacts was systematically associated with event boundaries and, therefore, a potential confounder on our EEG results, we calculated the time points where the amplitude of the EOG channel exceeded 3 SD and selected those whose absolute distance from the nearest boundaries was <10 s around the event boundaries time points. This value was then compared with a null distribution where the real EOG above-threshold time points were shuffled while maintaining the distance lengths between them (N = 1000). The real distances were compared with the null distribution by computing a z value, which was then converted to a p value using the normal distribution. A cutoff of α equal to 0.1 was used to assess statistical significance.

3.4 Results

3.4.1 Event segmentation and perceived event boundaries

Temporal points at which at least three external raters (of six) coincided in annotating a boundary were taken as indicative of a “real” event boundary in the movie. This approach resulted in an event segmentation model of 38 event episodes (Figure 3.1a), which was consistent with the range and the time shifts of the boundaries found in our previous study (Baldassano et al. 2017).

3.4.2 Movie free recall

Participants’ memory accuracy indicated that they were able to recall 51.4% of the encoded events on average (SD = 9.2%) (Figure 3.1b). Importantly, we also found that the temporal order of the episodic events at encoding was preserved at recall (Figure 3.1c). To statistically assess whether the order of events during movie watching was preserved during free recall, we computed Kendall rank correlation coefficients between each individual event temporal order and a simulated correct linear order. For all participants, the Kendall tau coefficient was positive and close to 1, indicating that the encoded temporal order of the events was highly preserved during their recall, thereby replicating

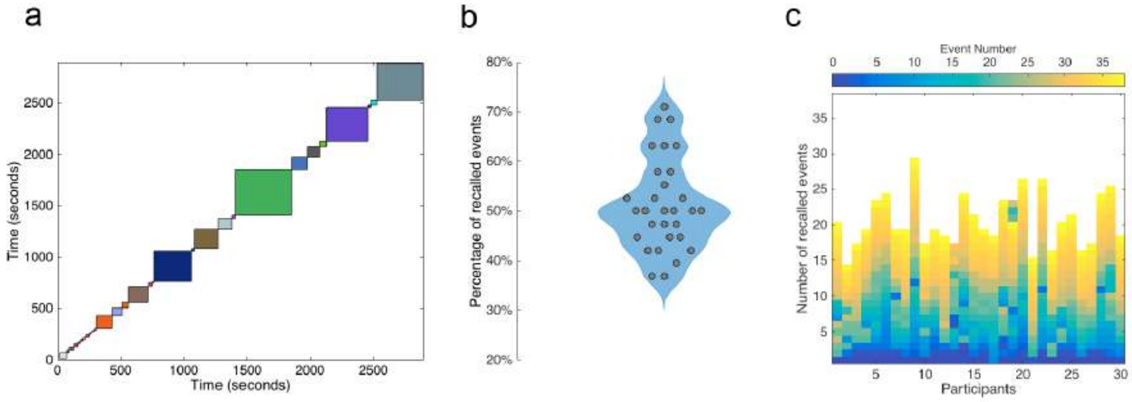


Figure 3.1: Event segmentation model and memory performance. a) Schematic representation of the event segmentation model derived from human annotations. Each color-coded square represents events during the 50 min movie and start/end of each event represents the boundary time points. b) Proportion of events that were later recalled by the participants in our sample (N = 30). c) Color-coded temporal order distribution of movie events that were recalled in the free recall task for each participant.

previous results (Chen et al. 2017) that free recall tends to preserve the temporal structure of the encoded memories.

3.4.3 Event segmentation model on the EEG data

Next, we tested whether patterns of EEG activity elicited by the 50 min movie exhibited the event structure hypothesized by our model (periods with stable event patterns punctuated by shifts between events). To address this issue at individual level, we computed a per time point spatial similarity analysis of the EEG data during the 50 min movie watching and calculated the degree of similarity values within each of the events (defined by the human-annotated event boundaries) (Figure 3.2a). To statistically assess the extent to which the EEG data fit the model, we averaged the similarity values within each of the 38 events and tested this value against a null distribution generated by running the same analysis 1000 times with a shuffled temporal order distribution of the events (Figure 3.2b). This analysis revealed that 22 of the 30 participants in our sample showed a higher degree of similarity values within events from the real segmentation model compared with their individual correlation value cutoff ($\alpha = 0.05$) from their null distribution (Figure 3.2c), and that this was significant at group level ($p < 0.05$; Figure 3.2d).

3.4.4 Shared event neural patterns across participants during movie watching

Having shown that EEG patterns of neural activity were structured according to a general event segmentation model during movie watching, we then tested the prediction that event EEG patterns should be shared across individuals (Chen et al. 2017). To address this question empirically, we computed Movie-Movie correlations by comparing patterns of each event from one participant with the

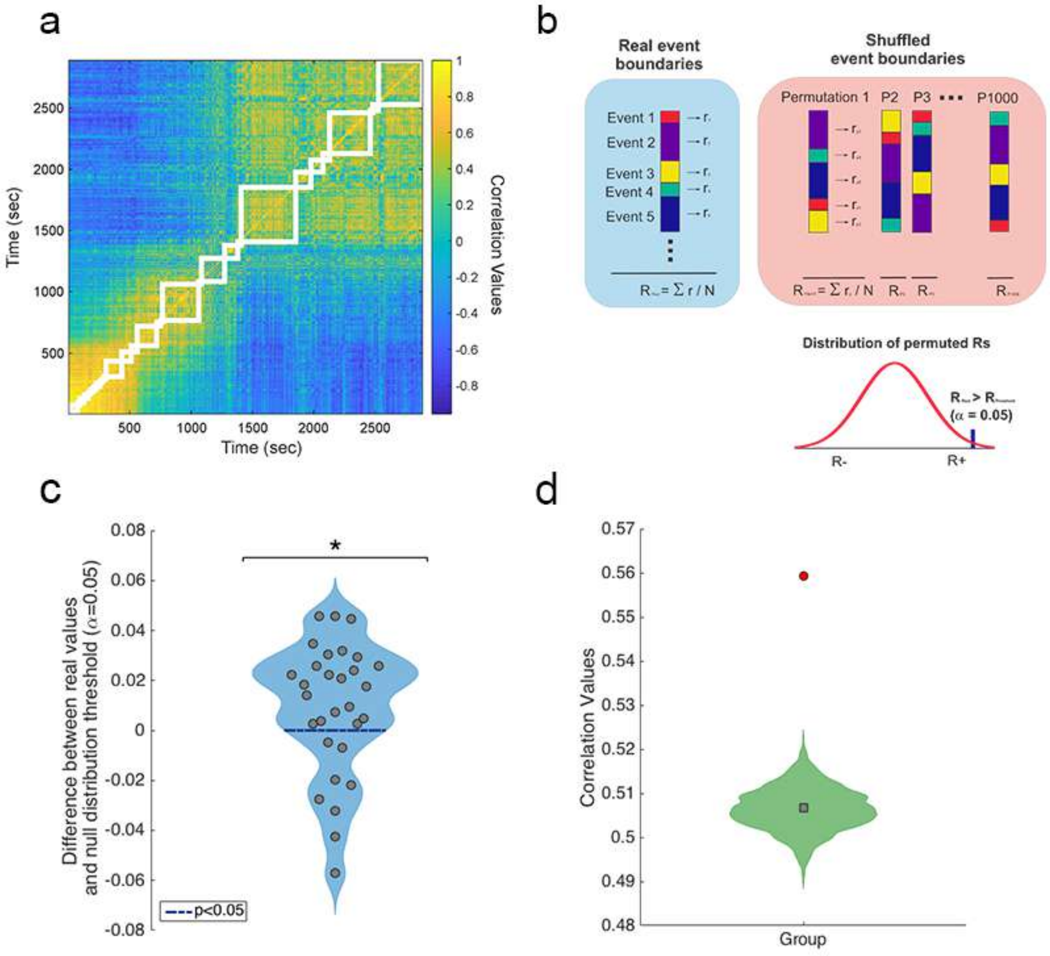


Figure 3.2: EEG neural patterns during movie watching and event segmentation model. a) A temporal correlation matrix was generated from raw EEG data for each of the participants (an example of one selected participant is depicted in this figure). The event segmentation model from human-labeled boundaries is overlaid in white. b) For each participant, the event segmentation model was used to calculate the averaged correlation values for pairs of time points within each event. A null distribution of correlations was obtained for random event boundaries by shuffling the order of the events of the segmentation model 1000 times. c) Single-participant distribution of the difference between the real within-event correlations and $\alpha < 0.05$ thresholds from the null distribution. *Significant at group level ($p < 0.05$). d) Red circle represents the true participant average. Green histogram represents the null distribution of the participant average. Gray square represents mean of the null distribution.

movie pattern for the same event averaged across the remaining participants. An averaged correlation value was obtained for each participant, and its statistical significance was assessed by comparing it with a random distribution obtained by shuffling the event order on the left-out participant. Confirming previous findings on fMRI data (Chen et al. 2017), we found that almost all of the participants (29 of the 30) showed a high degree of shared similarity EEG patterns with the group sample ($p < 0.05$ at group level) (Figure 3.3a,b). These results reveal not only that participants share brain patterns while being presented with the same stimuli but that their activity patterns evolve similarly over time given that they follow the same annotation structure. This analysis does not specifically test whether the annotated events have a coherent neural pattern (*e.g.*, high within-event pattern similarity), which is addressed in the analysis below.

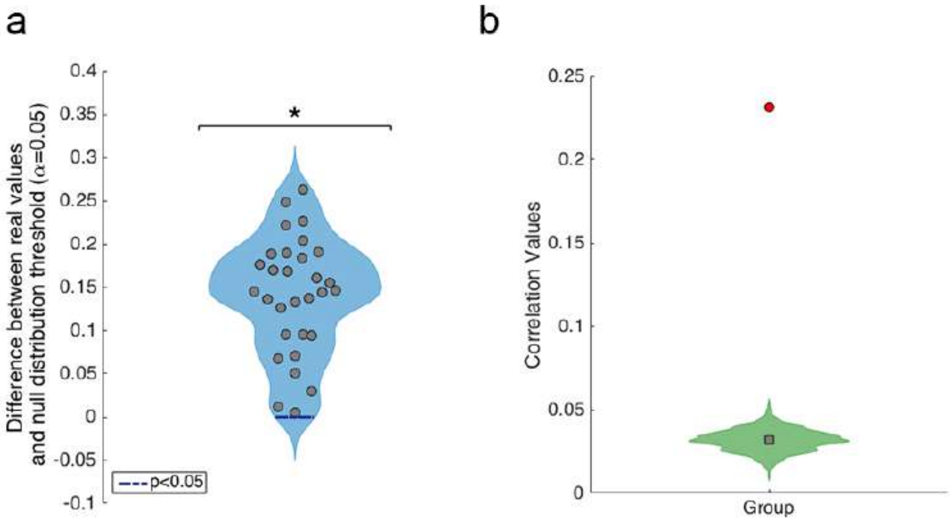


Figure 3.3: Between-participant pattern similarity during movie viewing. a) Intersubject correlation value derived from correlating the patterns for each event in each individual with the corresponding event patterns in the rest of the group, compared with an < 0.05 threshold from the null distribution. *Significant at group level ($p < 0.05$). b) Red circle represents the true participant average. Green histogram represents the null distribution of the participant average. Gray square represents mean of the null distribution.

3.4.5 EEG pattern similarity within and across events separated by boundaries

An important assumption derived from event segmentation theory is that patterns of neural activity elicited within an event should be more stable than neural patterns across events, thereby indicating that event neural representations change when boundaries are detected. To test this prediction in our data, we ran a point-to-point spatial similarity analysis throughout EEG segments of -10 to 10 s of averaged EEG trials around the boundary time point. The long EEG segments were then split into EEG epochs of 5 s each, thereby allowing us to examine the extent to which similarity values were higher for neural responses within events. More concretely, the similarity analysis was performed between three different pairs of temporal intervals in the data: preboundary time intervals (-10 to -5 s and -5 to 0s to the boundary), between-event time intervals (-5 to 0 and 0 to 5s to the boundary), and postboundary time intervals (0 to 5 s and 5 to 10 s to the boundary) (Figure 3.4a). The resulting similarity values for each condition and subject were then averaged, and differences were tested by means of a repeated-measures ANOVA. Notably, the results from this analysis revealed that similarity values differed between conditions ($F(2,58) = 14.43$, $p < 0.001$). Post hoc paired t test showed that within-event similarity, both before and after boundary, was higher than between-event similarity ($t(29) = 12.49$, $p < 0.001$ and $t(29) = 10.86$, $p < 0.001$, respectively) and that similarity values within preboundary and postboundary conditions were statistically equivalent ($t(29) = 1.99$, $p < 0.055$) (Figure 3.4b).

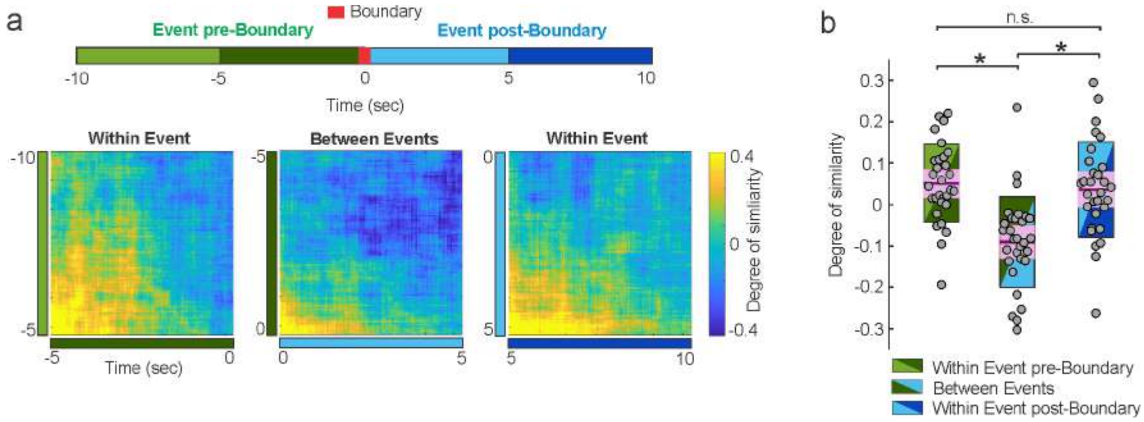


Figure 3.4: Neural pattern similarity within and across events during movie viewing. a) A time-resolved similarity analysis was calculated for pairs of samples over 20 s around boundaries, grouped based on whether the two samples fell before the boundary, on both sides of the boundary, or after the boundary. Time-resolved degree of similarity averaged over participants for EEG activity within events before the boundary, across events separated by boundaries, and within events after boundaries. b) Participant's degree of similarity for each of the event conditions depicted in a. For all boxplots, the central mark is the median, and the edges of the box are the 25th and 75th percentiles. $^*p < 0.05$; *n.s.*, $p > 0.05$.

3.4.6 Boundaries trigger rapid reactivation of the just-encoded event during movie viewing

Leveraged by previous findings indicating that explicit context shifts triggered rapid reinstatement of the just-encoded picture event sequence and that such reinstatement at boundaries promoted the formation of long-term memory for that event (Sols et al. 2017), we tested the prediction that neural reactivation may also support memory formation of the just-encoded event during much more subtle transitions between events during movie watching, providing converging evidence that memory reinstatement at event boundaries facilitates the storage of events into long-term memory. To address this issue, we computed a neural similarity analysis between EEG data epochs of 10 s preceding and following boundary time points and compared the resulting similarity values for events that were later recalled in the free recall task with events that were later forgotten. This analysis revealed that patterns $\sim$1.5 s after boundary were significantly more similar to patterns $\sim$5–10 s before boundary when these preboundary events were later recalled (Figure 3.5a). These findings provide evidence that neural reactivation is a mechanism supporting the formation of event episodic memories upon boundary detection during a continuous stream of stimuli.

3.4.7 Neural responses accompanying neural reactivation at boundaries

Although memory reactivation was found to take place rapidly upon boundary onset (*i.e.*, $\sim$1.5 s) in our study, research on ERPs has also revealed the existence of fast neural-evoked responses produced when the input directly disconfirms comprehenders' anticipations of upcoming narrative constituent structure. Specifically, this research used visual narrative picture sequences (comic strips) and showed that a left-lateralized anterior negativity ERP effect appeared between 500 and 700 ms to pictures that disrupted the constituent narrative structure of the sequence (Cohn et al. 2014). Thus, given that memory formation of a meaningful event may depend on the ability to perceive a narrative shift at a boundary (*i.e.*, segmentation) (Kurby and Zacks 2008), we asked whether perceived movie boundaries following events that were later recalled triggered a lateralized anterior negativity ERP component. To address this issue, we compared the ERPs time-locked to boundaries following events that were later recalled and forgotten, and we found that these two conditions showed a differential ERP in a time window of 600 –1400 ms after boundary onset, being more negative in polarity after boundaries following events that were later recalled (Figure 3.5b) with a left lateralized anterior scalp distribution (Figure 3.5c). Importantly, this ERP difference was not observed when the same analysis was performed at neural responses time-locked to boundaries preceding later recalled and forgotten events (Figure 3.5b), and these findings could not be attributed to a distinct proportion of events that were later recalled or forgotten following the boundary event either (Figure 3.7), indicating that the memory formation processes associated with memory formation had a retrospective nature when boundaries were detected. Furthermore, a source brain analysis revealed that activity from frontal, parietal, and medial temporal regions were involved in the ERP differences between conditions (Figure 3.5d), matching brain regions found to be associated with event boundary segmentation in our previous fMRI study (Baldassano et al. 2017). Together, these findings suggest that memory reactivation at event boundaries is accompanied by a rapid neural response signaling a shift between previous and current ongoing event information.

3.4.8 Neural reactivation during free recall

An intriguing finding in our previous fMRI study using the same movie was that the elicited patterns of neural activity associated with event segmentation during encoding were later reinstated during free recall (Baldassano et al. 2017). The extent to which these findings could be replicated using electrophysiological recordings may be relevant to open new venues for examining the neural mechanisms supporting event structure reinstatement patterns. To address this possibility, we adapted the approach implemented in our previous study based on HMM to the present EEG study. Briefly, the HMM approach implements a data driven segmentation search and returns the most probable division of a given signal to a given number of events. An important advantage of the HMM in the context of this study is that it provides a data-driven solution for how the ongoing pattern of neural activity may be sequenced into a given number of events. This is an attractive approach as it allows searching for the existence of patterns of neural activity related to complex event sequence structure in a flexible manner, as the algorithm can be applied to brain signals of different length. This is particularly relevant in the context of a free recall task, as in the current study, given that total recall length and per-event recall time length varied across participants and within participants, respectively (Figure 3.7a). Thus, for each participant, the HMM was used to estimate a 38-event segmentation of the continuous EEG data acquired during recall that most closely corresponded to the 38 neural event patterns elicited during movie watching. If, according to our previous findings using fMRI (Baldassano et al. 2017), participants' recall involved the reinstatement of neural patterns during encoding, we would expect event-elicited EEG activity during encoding and HMM-derived event-elicited EEG activity at recall to be very similar. To measure this, we correlated the EEG patterns elicited during encoding and recall and tested whether the resulting correlation value was

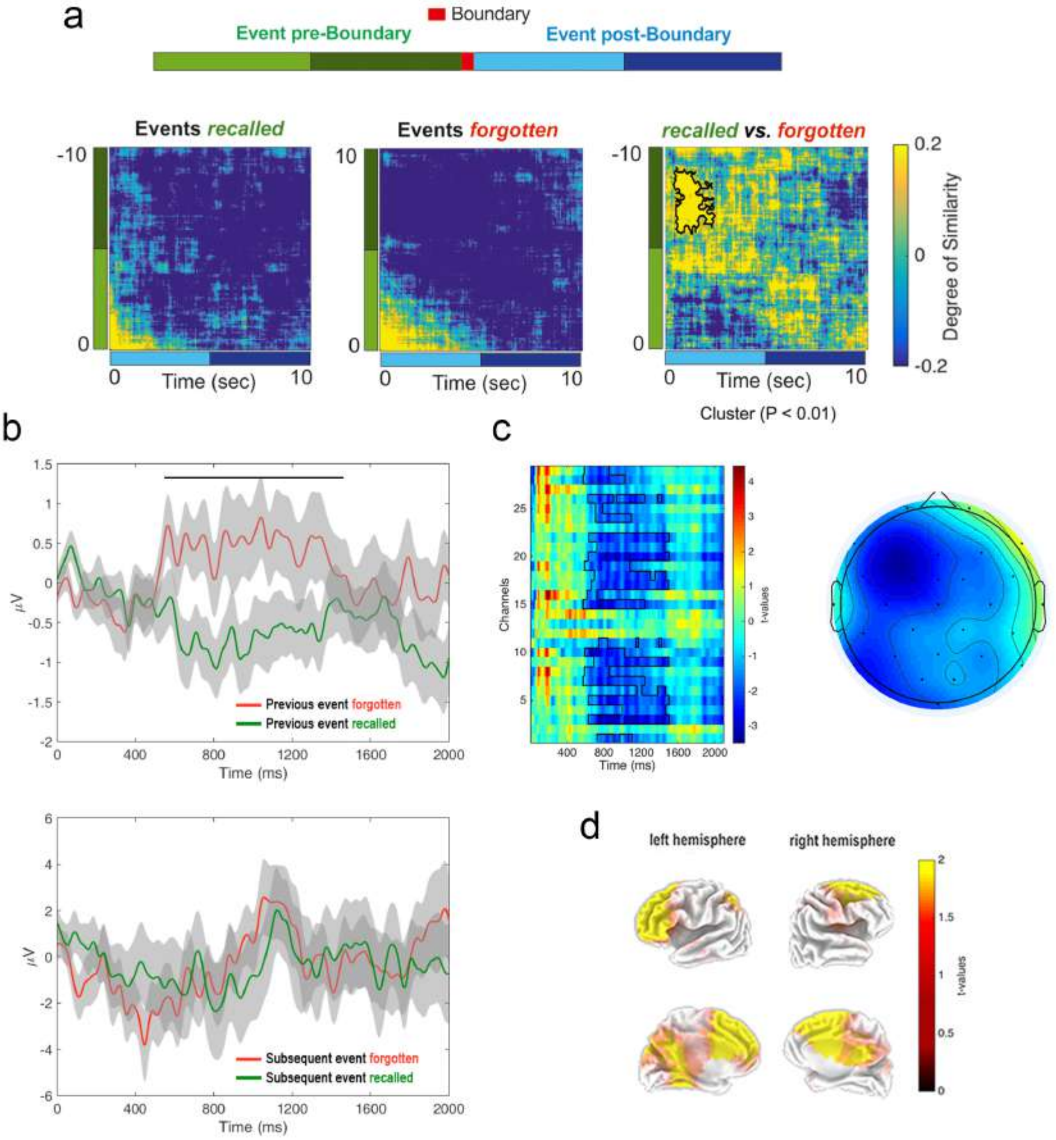
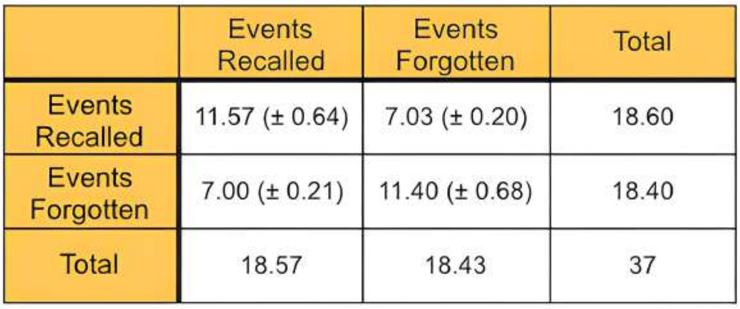


Figure 3.5: Rapid neural reactivation and event-related response at boundaries during movie watching. a) Time-resolved degree of similarity across event boundaries that followed events that were later recalled or forgotten. Right, Difference between similarity values for the two conditions. Statistically significant ($p < 0.05$, cluster-based permutation test) greater similarity was found across events for EEG at boundary onset (indicated by a black thick line). b) ERPs elicited at boundary onset during movie watching as a function of whether the previous (above) or subsequent (below) event was recalled or forgotten in the subsequent recall task. Thick lines indicate the averaged ERPs over the 29 scalp electrodes across participants. Shaded area represents SEM of the participants' sample. Thick black line indicates the timing of the significant cluster between ERP conditions ($p < 0.05$, cluster-based permutation test). c) Point-to-point ERP difference at boundary onset as a function of whether previous events were later recalled or forgotten. Differences are expressed in t values (paired t test). Thick black line indicates cluster of significance. Right, Scalp ERP representation of the ERP difference between the two conditions averaged over time points within the significant cluster. d) Brain sources of the ERP difference observed at boundary onset between recall and forgotten conditions.



	Events Recalled	Events Forgotten	Total
Events Recalled	11.57 (± 0.64)	7.03 (± 0.20)	18.60
Events Forgotten	7.00 (± 0.21)	11.40 (± 0.68)	18.40
Total	18.57	18.43	37

Figure 3.6: We created a table of contingency for each of the participants to assess the possibility that recalled or forgotten events during movie-watching were nonuniformly preceded or followed by either recalled or forgotten events. For each participant, we performed a Fisher's exact test to statistically assess for an unequal distribution of events. This analysis resulted in no significance ($p > 0.05$) for all participants, thereby indicating that the distribution of recalled and forgotten trials was uniform.

higher than in a null distribution obtained by shuffling the duration of the encoding events before computing the mean patterns of each event before running the HMM on recall data. We found that the correlation values between movie and recall could not be attributed to chance at group level ($p < 0.01$; Figure 3.5b). This result extends previous fMRI findings (Baldassano et al. 2017), demonstrating that memory recall is supported by the reactivation of the electrophysiological patterns elicited during movie viewing.

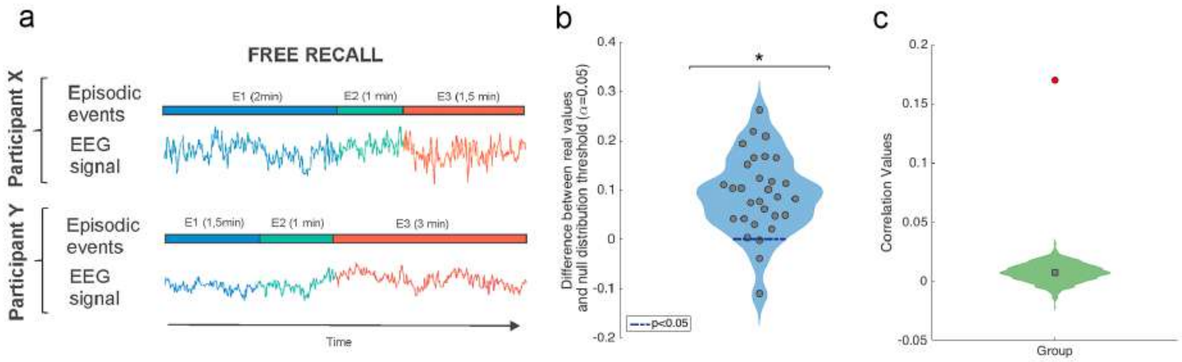


Figure 3.7: Movie event memory reactivation during verbal recall. a) Illustration of how 2 participants' recall lengths varied for the same three events. Using an HMM approach, we searched for reinstatement of EEG neural event patterns despite these differences' lengths. b) EEG correlations between event segmentation model patterns during movie watching and recall activity derived from HMM-estimated events were computed. A null distribution created by randomly permuting the order of the events at encoding before deriving the HMM-estimated events at recall was used to attest for statistical significance ($p < 0.05$). Red circle represents the true participant average. Green histogram represents the null distribution of the participant average. Gray square represents mean of the null distribution.

3.4.9 Possible eye movement artifacts near event boundaries

An important concern that needed to be addressed to attest the validity of our results was the possibility of eye movements being systematically associated with event boundaries, which could potentially account for, or obscure, the EEG results. To discard this possibility, the number of EOG artifacts whose absolute distance from the nearest boundaries was smaller than 10 s around the event boundaries, time points were selected and compared with a null distribution where the real EOG above-threshold time points were shuffled while maintaining the distance lengths between them (N = 1000). The real distances were compared with the null distribution by computing a z value, which was then converted to a p value using the normal distribution. At encoding, we found that the distribution of real EOG above-threshold activity was not statistically different from the averaged null distribution; 27 of 30 participants had p values > 0.05; and at the group level, the obtained p value was 0.5, which indicates that there is no evidence that EOG artifacts elicited during movie viewing are associated with boundaries (Figure 3.8a). A similar analysis was conducted during recall; but considering the distances between EOG above-threshold activity and boundaries time points obtained using the event segmentation HMM-based approach. This analysis revealed that 30 participants had p values > 0.05; and at the group level, the obtained p value was 0.8, which confirmed that potential eye movement artifacts were not associated with event boundaries during recall either (Figure 3.8b)

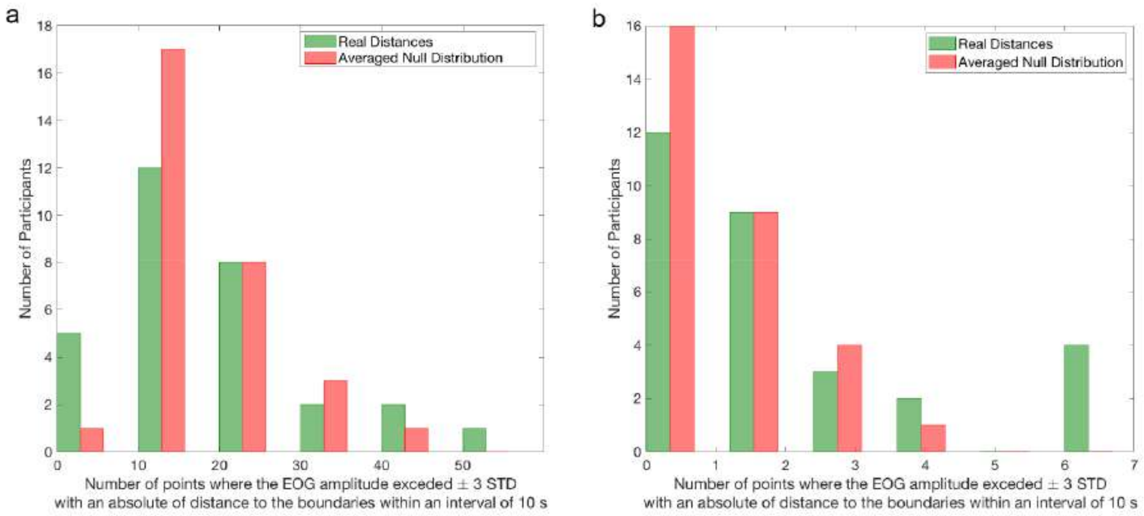


Figure 3.8: Relationship between eye movements and boundaries during movie watching and recall. To statistically assess whether the existence of potential eye movement artifacts was associated with boundaries, we calculated the time points where the amplitude of the EOG channel exceeded 3 SDs and selected those whose absolute distance from the nearest boundaries was <10 s. This value was compared with a null distribution where the real EOG above threshold time points was shuffled while maintaining the lengths between them (N = 1000). a) At encoding, we found that the distribution of real EOG activity (green) was not statistically different from the averaged null distribution (red). The real distances were compared with the 1000 null distances by computing a z value, which was converted to a p value using the normal distribution; 27 of 30 participants had p values > 0.05; and at the group level, the obtained p value was 0.5, which indicated that EOG activity above a given threshold during movie watching was not associated with boundaries. b) A similar analysis was conducted during recall, but considering the distances between eye movements and boundaries time points obtained using the event segmentation algorithm. This analysis revealed that 30 participants had p values > 0.05; and at the group level, the obtained p value was 0.8, which confirmed that potential eye movement artifacts were not associated with boundaries during recall either.

3.5 Discussion

Our results provide the first evidence of electrophysiological signatures related to how event segmentation during movie viewing shapes memory formation. They show that patterns of neural activity recorded from the scalp EEG while viewing a 50 min movie fit with an event segmentation model of episodic events punctuated by rapid transitions of content (*i.e.*, event boundaries). We observed that these event-specific patterns of neural activity were reinstated at later recall, thereby corroborating the idea that the event segmentation process shaped memory formation of a continuous stream of stimuli into a structured memory representation that can be accessed long-term. Leveraged by the fine-grained temporal resolution of the EEG data, we showed that event memory formation during movie viewing was mediated by its rapid reactivation at event boundaries and that memory reactivation was accompanied by a left-lateralized anterior negativity ERP effect time-locked to the boundary, which likely reflects the effective detection of a context switch between the current and just-encoded event. These findings indicate that the successful encoding of an episode is regulated by two neural mechanisms that act within the first 2 s after an event boundary.

Why would memory reactivation be advantageous during the encoding of a continuous stream of stimuli? Although event segmentation provides a framework to examine how continuous experience can be chunked into a set of discrete episodes in memory through the detection of event boundaries, it does not account for how this sequence of episodes can be integrated into a memory structure that preserves the temporal structure during later recall. Memory reactivation at event boundaries may represent a way to promote temporal event memory organization across boundaries as it may serve to promote the strengthening, or chunking, of that just-encoded event, but it also may help promote binding across boundary episodes as a result of the contemporaneously coactivation of the past and present events (Sols et al. 2017). The extent to which memory reactivation at event boundaries serves to promote the encoding of unique events into memory, the integration of different events into a temporally organized memory structure or both is difficult to disambiguate in our study as participants memory accuracy was obtained through a free recall task, which relies on retrieval processes heavily dependent on clustering properties of the encoded material, such as semantic similarity or temporal proximity Polyn, Norman, and Kahana 2009).

Speculatively, it could be argued that memory reactivation at event boundaries could represent a way to account for how different event episodes that shared contextual semantic properties can be integrated. In support of this hypothesis, previous fMRI studies have shown that temporally extended events sharing contextual information were evaluated as if they appeared closer in time during recall and that this was related to increased hippocampal similarity between these events during encoding (Ezzyat and Davachi 2011). Interestingly, this effect was only observed for when events that shared contexts were separated by event boundaries during their encoding, suggesting the possibility that neural mechanisms triggered at boundaries were at least partially responsible for memory integration (*e.g.*, memory reactivation). Another set of research studies have emphasized the relevance of memory reactivation to explain how different episodes are integrated as a function of the degree of their overlapping content to allow generalization (Schlichting and Preston 2015). These studies have shown that memory reactivation is elicited when elements of the experience partially mismatch with stored memory representations, supporting integrative encoding online (Shohamy and

Wagner 2008).

An open question is which specific mechanisms triggers memory reactivation at event boundaries. Advancing on this issue is not trivial given the diverse ranges of stimulus used in event cognition literature: for instance, text narratives (Zwaan 1996), short video clips (Ben-Yakov and Dudai 2011; Ben-Yakov, Eshel, and Dudai 2013), or item sequences (DuBrow and Davachi 2013). In an attempt to accommodate the literature on this topic, Clewett and Davachi 2017 suggested that event boundaries represent moment-to-moment fluctuations in external and internal contextual states during continuous encoding. In our study, such fluctuations could be understood as moments in time when an internal representation derived from an accumulated contextual encoding suddenly shifts at the start of a novel scene with a change in spatial location, characters, or goals. Interestingly, this effect was only observed for when events that shared contexts were separated by event boundaries during their encoding, suggesting the possibility that neural mechanisms triggered at boundaries were at least partially responsible for memory integration (*e.g.*, memory reactivation) (Griffiths and Fuentemilla 2020). Another set of research studies have emphasized the relevance of memory reactivation to explain how different episodes are integrated as a function of the degree of their overlapping content to allow generalization (Schlichting and Preston 2015). These studies have shown that memory reactivation is elicited when elements of the experience partially mismatch with stored memory representations, supporting integrative encoding online (Shohamy and Wagner 2008)). Interestingly, we found that these moments in time were followed by a left-lateralized anterior negative ERP effect, specifically for when the previous event was later recalled but not for those that were forgotten. The fact that this specific ERP response accompanied memory reactivation after an event boundary lends support to the notion that it could reflect a neural process that may be necessary to trigger neural reactivation. However, this idea should be taken cautiously as our data do not provide a quantifiable dependency between the two, other than differences in their temporal onset.

Similarly, it would be important to delimit the representational nature that encompasses rapid memory reactivation at event boundaries. Despite the relevance of this question, our current approach, based on scalp EEG activity recordings from the scalp, is blind on whether the increased neural similarity at event boundaries to recalled events may reflect the representation of episodic details of the just-encoded event or whether, indeed, it encompasses the reactivation of the gist-based memory representation of the encoded event, or both. Disambiguating between these possibilities is not trivial when using scalp EEG recordings for at least two reasons. First, the intrinsic temporal correlation of the EEG data did not allow us to discern whether memory reactivation was associated with the entire neural patterns elicited during the preboundary event, as our findings were based on the comparison of two memory conditions that showed increases in neural similarity for time points surrounding the boundary (see Figure 3.5a). And second, as opposed to data from fMRI that can link the neural responses to known representational hierarchy coding along the visual stream (*e.g.*, Baldassano et al. 2017), we are agnostic on how the differential gradient of specific versus abstract memory representations may be distinguished, if they may, in the scalp EEG signal.

In a series of fMRI experiments, Ben-Yakov and Dudai (Ben-Yakov and Dudai 2011; Ben-Yakov, Eshel, and Dudai 2013) revealed the importance of studying event offset brain activity in humans at the end of movie clips to understand how episodic memories are formed during the stream of a continuous audiovisual stimulation. These studies, together with those studying abrupt switches between stimulus category and task (DuBrow and Davachi 2014), and recent studies of event boundaries in movies (Baldassano et al. 2017; Ben-Yakov and Henson 2018), offered converging evidence for the specificity and sensitivity of the coupling of the hippocampus to event boundaries during movie viewing. In the current study, we found that the brain sources of the left-lateralized anterior negative ERP effect associated with memory formation at boundaries of the just-encoded event episode included frontal, parietal, and medial temporal lobe regions. These regions highly overlapped with brain regions found in our previous fMRI findings of hippocampally linked event boundaries (Baldassano et al. 2017). The similarity of these sources represents strong evidence that our approach was suitable for identifying the engagement of the same brain network and informing about the temporal properties of their engagement using noninvasive electrophysiological recordings.

In naturalistic scenarios, the study of the recollection of memories of one's past may vary substantially across individuals and within subjects as a function of task contexts. This originates an important challenge in our search for the neural underpinnings, supporting the remembering of autobiographical memories. The implementation of data-driven modeling approaches, such as the ones offered by HMM used in the current study, may foster interesting possibilities in this endeavor. Indeed, being able to identify the reinstatement of memory events from a 50 min movie viewing using HMM extends previous fMRI findings (Baldassano et al. 2017). Our work, however, is the first to show that HMM can be used to model electrophysiological signals, thereby proving its usefulness to test predictions of how perception and memory are supported by brain mechanisms that act at fine-grained temporal resolution. Nevertheless, future work may extend the current approach by examining how HMM can be implemented in electrophysiological signal to search for unknown patterns. Notably, our approach was successful in identifying the appearance of a known pattern during recall extracted from encoding. It would be interesting to discern which electrophysiological features are relevant during encoding, thereby providing a way to contribute to findings set out from our previous fMRI studies (*e.g.*, Baldassano et al. 2017).

Understanding how memories are formed and structured in real-life requires the characterization of neural mechanisms that take place online, during the ongoing encoding of continuous naturalistic stimuli, as our experience unfolds over time. Investigating how memories are formed during audiovisual narratives, such as long movie clips, may provide a valuable approach to bring testable predictions derived from animal and theoretical neuroscience into real-life settings. The current experiment assessed whether memory reinstatement, a neural mechanism critical for memory formation and consolidation, took place under these ecologically valid experimental circumstances. By showing that this is the case, our findings offer insights into how the brain shapes the unfolding experience into long-term memory that can be generalized to real-life.

Chapter 4

Study 2: Cortico-hippocampal ripple-based coordination during naturalistic encoding

4.1 Summary

Effective communication between the hippocampus and cortical areas during the encoding of an event is crucial for memory formation. SWRs, highly coordinated and precisely timed neural events, have been implicated in facilitating this flow of information. While extensively studied in rats, recent evidence suggests the presence of ripples in humans, supporting the formation and retrieval of associative memories. This study aimed to understand the mechanisms underlying ripples during a naturalistic encoding task in humans. Intracranial electrophysiological data were recorded from cortical and hippocampal electrodes of epilepsy patients watching a 50-minute movie. The results revealed a cortico-hippocampal ripple mediated interaction throughout an event, suggesting a role of ripples in facilitating the binding of disparate memory elements across cortical areas. Additionally, ripple activity increased at hippocampal event boundaries and within events at the cortical level, reflecting distinctive patterns of information processing during different temporal periods. These findings enhance our understanding of memory encoding mechanisms and highlight the involvement of ripples in event segmentation.

4.2 Introduction

In the process of encoding an event, the effective communication between the hippocampus and cortical areas is of utmost importance for memory formation (Baldassano et al. 2017; Geerligs et al. 2022; Ranganath et al. 2005; Reagh and Ranganath 2023). Among the different patterns of neural activity, SWRs have emerged as a distinct neural signature involved in the transmission of information within the brain. SWRs are characterized by sharp, high-frequency neural oscillations that occur in a highly coordinated and precisely timed manner (Bragin et al. 1999). Extensive studies conducted in rats have demonstrated that these transient events are accompanied by widespread activations in both cortical and subcortical regions (Karimi Abadchi et al. 2020; Gomperts, Kloosterman, and Wilson 2015). It is believed that ripples reflect the coordinated activity between the hippocampus and neocortex, facilitating efficient interaction during memory formation and consolidation (Todorova and Zugaro 2020; Vaz et al. 2019; Norman et al. 2021; Dickey et al. 2022). Recent studies have provided evidence for the occurrence of this specific type of neural activity in the human hippocampus (Norman et al. 2019; Vaz et al. 2020; Axmacher, Elger, and Fell 2008), suggesting its potential role in facilitating the formation and retrieval of event memories in humans too (Kunz et al. 2022; Sakon and Kahana 2022). However, whether human hippocampal-neocortical coordination is mediated by ripple events during naturalistic scenarios, where episodic information unfolds continuously, remains unexplored.

Understanding the cognitive and neural underpinnings of episodic memory formation in realistic environments is largely influenced by the view that the continuous experience is rapidly transformed into discrete episodic units via the detection of event boundaries (Zacks et al. 2007). Indeed, event segmentation affects not only our perception of an experience, but its subsequent organization in long-term memory (Kurby and Zacks 2008; Radvansky 2012; Sargent et al. 2013), such that elements within an event are bound together more cohesively than elements across events (Ezzyat and Davachi 2011; DuBrow and Davachi 2013; DuBrow and Davachi 2014; Horner et al. 2016). Processing at event boundaries has been associated with improved long-term memory for the corresponding information (Newtson and Engquist 1976; Schwan, Garsoffky, and Hesse 2000; Schwan and Garsoffky 2004) and the hippocampus has been shown to be particularly active and engaged during these moments (Ben-Yakov, Eshel, and Dudai 2013; Baldassano et al. 2017; Ben-Yakov and Henson 2018). On the other hand, other cortical areas seem to be more sensitive to the representation of information within an event (Reagh and Ranganath 2023). Based on this distinct pattern of information processing, we postulated that similar dynamics should be expressed in ripple activity.

To study this, we recorded intracranial electrophysiological data from frontal cortex, temporal cortex and hippocampus of patients undergoing treatment for pharmacologically intractable epilepsy, while watching a 50 min long movie. Previous research has focused on the detection of ripples during sleep or during awake periods where participants had to encode discrete stimuli. In this study, we investigate, for the first time, the occurrence of this neural activity type within a continuous and dynamic stream of information. To ensure the comparability of the identified ripples with those previously reported in humans, we conducted a comprehensive analysis of various properties, including power, duration, and inter-ripple interval. We also calculated the probability of hippocampal ripples being modulated by the phase of delta band activity as such a temporal interaction was suggested to be relevant for the coupling of ripples with neocortical activity (Maingret et al. 2016). Building upon earlier evidence of widespread ripple occurrence across the cortex, we examined whether ripples co-occurred in diverse cortical areas throughout the encoding of an event and investigated their impact on activity in other regions. To assess if ripple activity would reflect the specific hippocampal recruitment at event boundaries seen in previous studies (Ben-Yakov, Eshel, and Dudai 2013; Baldassano et al. 2017; Ben-Yakov and Henson 2018) we explored how the ripple rate fluctuated around boundaries and within event. Overall, our results shed light on the intricate mechanisms underlying memory encoding and provide insights into the role of ripples in event segmentation. Our findings provide compelling evidence for a hippocampal-cortical ripple mediated interaction throughout the progression of an event, and a hippocampal ripple recruitment at event boundaries. These results imply that sharp-wave ripples play a potential facilitative role in binding diverse memory elements represented across distinct cortical areas, enabling the formation of coherent representations.

4.3 Materials and Methods

4.3.1 Data collection

We tested 11 human subjects who were undergoing treatment for pharmacologically intractable epilepsy at Hospital Clínic – IDIBAPS in Barcelona. Of those, 1 patient had to be excluded due to artifactual data. Prior to performing the task, all participants were thoroughly briefed on the specificities of the task, ensuring they had a comprehensive understanding of the objectives, procedures, and potential risks involved. Each participant was provided with a consent form, which they attentively reviewed and willingly signed, demonstrating their informed consent to participate in the study.

Patients were surgically implanted with intracranial depth electrodes for diagnostic purposes, with the goal of isolating their epileptic seizure focus for potential subsequent surgical resection. The exact electrode numbers and locations varied then across subjects and were determined solely by clinical needs. The recordings were performed using a clinical EEG system (Natus Quantum LTM Amplifier) with a 2048Hz sampling rate and an online bandpass filter from 0.1Hz to 4000Hz. Intracerebral electrodes (Microdeep, DIXI Medical) were used for recordings. Each multielectrode had 8 to 18 contacts, spaced 5 mm and 1 to 2 mm long with a diameter of 0.8 mm.

4.3.2 Experimental Design

The experiment was conducted in a sound-attenuated room in the hospital, with participants sitting upright in a comfortable chair or on their bed. Participants were asked to watch the first 50 min of the first episode of *BBC's Sherlock*, dubbed in Spanish, as done previously in Silva, Baldassano, and Fuentemilla 2019. Participants were informed that a subsequent recall memory test would follow. After the movie, participants had some time to rest (5-10 min) before the test began. During the test, they were asked to freely recall the episode without cues while being recorded using an audio recorder placed on the overbed table next to the laptop computer. The audio files were later analyzed to access participants' length of the recall. The experimental design was implemented on PsychoPy (Peirce et al. 2019) and presented on a 13-inch portable computer, placed on the overbed table at approximately 60 cm distance in front of the patients.

4.3.3 Event boundary annotations

The event model validated in Silva, Baldassano, and Fuentemilla 2019 was used for the current analysis. This model is composed by 38 events (minimum = 4 s, maximum = 444 s, and mean = 76.02 s) and it was constructed by having six external participants annotate the temporal point at which they felt "a new scene is starting; these are points in the movie when there is a major change in topic, location or time." The final model was built based on boundary time points that were consistent across observers.

4.3.4 Verbal recall analysis

The audio files from the free verbal recall were analyzed by a laboratory member who was a proficient Spanish speaker, using the list of events from the event model mentioned in the previous section. An event was counted as recalled if the participant described any part of that scene.

To statistically assess whether the order of events during movie watching was preserved during free recall, we computed Kendall rank correlation coefficients between each individual event temporal order and a simulated correct linear order. A positive Kendall tau coefficient close to 1 indicates that the encoded temporal order of the events was highly preserved during their recall.

4.3.5 Electrode localization and selection

The presence of electrodes in the respective brain areas was assessed with the examination of a computed tomography (CT) and (post-electrode removal) Magnetic Resonance Imaging (MRI) T1 scans. Cerebral atlases of each patient were obtained with the parcellation of the preoperatory T1 using Freesurfer (https://surfer.nmr.mgh.harvard.edu). The CT was co-registered to the T1 and contact tags and names were placed manually using fieldtrip's toolbox (https://www.fieldtriptoolbox.org/). Selection of channels was done in native space to prevent errors due to distortions.

To eliminate potentially system-wide artifacts or noise and to better sense ripples locally, we applied bipolar re-referencing between pairs of neighboring contacts. The channels of interest were selected based on the following criteria: if more than one channel was eligible, we privileged the channel that had an adjacent distal referencing contact also in that region; if this was not possible then an adjacent white matter electrode was selected; in the case where more than one pair of adjacent channels were eligible, we selected those that had the least amount of epileptic activity according to visual inspection.

Based on the above mentioned anatomical and functional criteria, one pair of hippocampal and one pair of temporal cortex depth electrode contacts was selected for each of the ten participants. One pair of frontal cortex electrodes was also selected for six out of the ten participants, as the missing four did not contain any electrode on that desired area.

4.3.6 Intracranial EEG preprocessing and Ripple Detection

Intracranial analyses were performed to identify ripples and examine the wide effects of ripples on local field potentials. In order to detect ripples, the procedure applied in Vaz et al. 2019; Vaz et al. 2020 was used. First, the EEG signal was bandpass filtered in the ripple band (80-120 Hz) using a second order Butterworth filter. Then a Hilbert transformation was applied to extract the instantaneous amplitude within that band. Events were selected if the Hilbert envelope exceeded 2 standard deviations above the mean amplitude of the filtered traces. Only events that were at least 25ms in duration and had a maximum amplitude greater than 3 standard deviations were retained as ripples for analysis. Adjacent ripples separated by less than 15ms were merged.

Simultaneously, an automated event-level artifact rejection (Vaz et al. 2019; Vaz et al. 2020) was applied in order to remove system level line noise, eye-blink artifacts, sharp transients, and interictal epileptiform discharges (IEDs), which can be mistakenly characterized as ripples after high pass filtering. To do so, we calculated a z-score for every time point based on the gradient (first derivative) and amplitude after applying a 250Hz high pass filter. Any time point that exceeded a z-score of 5 with either gradient or high frequency amplitude was marked as artifactual, such as 200ms before and after each identified time point.

All data and identified ripples were visually inspected to ensure that the above methodology reliably identified ripples and excluded IEDs and high frequency oscillations associated with IEDs. This procedure also allowed us to reject any channel with an excess of artifactual activity.

For each ripple, we extracted its peak time as the time point at which the band-pass signal was highest; the ripple duration, as the time difference between the start and end time of a given ripple; and the inter-ripple interval (IRI) as the time difference between the onset of two consecutive ripples. To depict the time-domain signal, we extracted the raw LFP traces, the traces filtered in the ripple band (80-120Hz) and the time-frequency-domain power spectrum (using Morlet wavelets with 7 cycles at 50 logarithmically spaced frequencies between 1 and 200 Hz and plotted from 60 to 140Hz), within -50 to 100ms around each ripple.

4.3.7 Ripple phase locking to ongoing neural oscillations at the delta band

To investigate whether ripples were locked to particular phases of delta oscillations (0.5 to 4Hz) we filtered the signal using a two-pass Butterworth filter and extracted the instantaneous phase using the Hilbert transform at the onsets of each ripple. To assess phase consistency across ripples we computed inter-trial phase coherence (ITPC) values across ripples for each participant. ITPC spans from 0 to 1, with 1 corresponding to a perfect intertrial coherence (*i.e.*, the same phase on each trial onset).

To assess statistical significance of ripple-phase coupling, we compared the empirical values against 1001 surrogate values computed by permuting the inter-ripple interval distribution (*i.e.*, permuting the time differences between the onset of two consecutive ripples), for each participant. We computed the P-value of the empirical ITPC z-value in comparison to the surrogate ITPC z-values as P = 1 - rank, where rank is the fraction of surrogate values that were smaller than the empirical value, with an alpha of 0.05.

4.3.8 iEEG spectral power during ripples

To assess whether hippocampal/cortex ripples were associated with significant changes in LFP power in cortex/hippocampus, respectively, we computed ripple-aligned time frequency-resolved power spectrograms (Kunz et al. 2022). For that we computed the time-frequency spectrograms across the entire recording using Morlet wavelets with 7 cycles at 50 logarithmically spaced frequencies between 1 and 200Hz. Power values were z-scored across time for each frequency. Values around each hippocampal ripple (±3s) were extracted and time points with IEDs were excluded (*i.e.*, set to NaN). Finally, power z-values values were averaged across ripples and smoothed with a Gaussian filter across time (kernel length, 0.2s). This procedure was computed individually for each participant and then averaged across participants. For depiction where we truncated the spectrogram ±0.5s around the ripple peak time point.

To statistically evaluate the validity of the power spectrum we performed a cluster-based permutation test (1000 surrogates) across channels in which we first applied a one-sample t-test to the empirical data, separately for each time–frequency bin, and identified contiguous clusters of time–frequency bins in which the uncorrected P-value of the t-test was significant ($\alpha = 0.05$). Then for each cluster, we computed an empirical cluster statistic by summing up all t-values being part of that cluster. The empirical cluster statistics was compared against surrogate cluster statistics, obtained by flipping the sign of the power values of a random subset of the spectrograms, performing exactly the same steps as for the empirical data, and keeping only the maximum cluster. The empirical cluster statistic was considered significant if it exceeded the 95th percentile or if it fell below the 5th percentile of all surrogate maximum cluster statistics.

4.3.9 Ripple cross-correlation between brain regions

To examine the hippocampal-neocortical coordination of ripple activity, we computed cross-correlations between the ripple time series of the hippocampal channel and the time-series of the cortex channels (composed of zeros and ones where ones indicate the ripple periods) (Kunz et al. 2022). A maximum time lag of ±1s was considered, as most ripples were expected to occur close together in time, to compute cross correlations through the use of built-in MATLAB's xcorr function. The cross-correlations were computed for each participant separately, smoothed with a gaussian filter (kernel length of 0.2s) and z-scored across time lags.

Statistically validity was assessed by performing a cluster-based permutation test (1000 surrogates) across channels. First a one-sample t-test was computed on the empirical data, separately for each time lag, and contiguous clusters of time lags were identified based on if the uncorrected P-value of the t-test was significant ($\alpha = 0.05$). Then for each cluster, we computed an empirical cluster statistic by summing up all t-values being part of that cluster. The empirical cluster statistics was compared against surrogate cluster statistics, obtained by flipping the sign of a random subset of the correlation series, and then performing the same steps as for the empirical data, keeping only the maximum cluster. The empirical cluster statistic was considered significant if it exceeded the 95th percentile or if it fell below the 5th percentile of all surrogate maximum cluster statistics.

4.3.10 Ripple rate during the encoding of movie events

The analysis of the ripple rate during the encoding of movie events was assessed by counting the number of ripples that occurred within each event, for each participant. This value was normalized by the length of the event, and then the resulting normalized ripple count was averaged across events. To evaluate the extent to which the number of ripples during the encoding of an event determined its successful recall at the later verbal recall test, for each participant, we split the events that were later recalled and forgotten and obtained an averaged measure of ripple count for each condition, which was then compared by using a two-sample t-test, with significance threshold set as an alpha of 0.05.

4.3.11 Ripple rate at movie event boundaries

To assess how ripples fluctuated around event boundaries we computed a peri-ripple time histogram of ripple events across the different event boundaries. We used 300-ms time bins starting from –2 to 2 s relative to ripple onset, and for visualizing purposes, smoothed it by a 5-point triangular window. This results in an estimate probability of observing a ripple at each timepoint and can then be averaged across participant.

The empirical ripple rates were compared against 1000 surrogate values computed by computing peri-stimuli histograms as above but by shuffling the temporal order of the events, while maintaining their lengths, resulting in ripple rates that corresponded to within event windows, for each participant. We computed the P-value of the empirical rates z-value in comparison to the surrogate values as P = 1 - rank, where rank is the fraction of surrogate values that were smaller than the empirical value, for each time-point surrounding a boundary, with an alpha of 0.05. The p-values were later FDR corrected.

4.4 Results

4.4.1 Ripples characteristics during the encoding of movie events

To investigate the presence and the functional role of ripples during the encoding of naturalistic stimuli we recorded electrophysiological activity from intracranial electrodes implanted in epileptic patients undergoing presurgical monitoring, while they watched a 50min long movie and performed a free verbal recall task. The free verbal recall task allowed us to assess how many and which events participants correctly encoded. Even though some of the patients showed poor performance in the recall test, on average, we found that most of the participants were successful in recalling the encoded events from the movie (M = 40.79%, SD = 11.18%), and were accurate in maintaining the order in which the events were presented in the movie during recall (mean Kendall $\tau = 0.7366$, $p<0.001$). These data replicate previous results with healthy participants (Silva, Baldassano, and Fuentemilla 2019).

We selected one hippocampal, one temporal and one frontal cortex electrode per participant, which were mostly located in the anterior portion of all regions, to conduct our analysis (Figure 4.1a,b). Following previous ripple-detection methods (Vaz et al. 2019; Vaz et al. 2020) we recorded a total of 5288 hippocampal ripples and 4756 temporal cortex ripples across all participants and 2965 frontal cortex ripples across the six participants with electrodes in that brain region. Crucially, IEDs were excluded to ensure that the ripples identified were not of pathological nature. The identified ripples reflected a number of properties, such as peak of power of about 90Hz (Figure 4.1d,e,f) or a mean duration around 35ms (Figure 4.1g,h,i), consistent with previous human studies (Axmacher, Elger, and Fell 2008; Norman et al. 2019; Vaz et al. 2019; Kunz et al. 2022).

We next analyzed whether ripples occurred predominantly during specific phases of delta band activity (0.5-4Hz), such as in previous findings (Axmacher, Elger, and Fell 2008; Kunz et al. 2022). We found that ripple occurrence locked to specific phases of the delta rhythm (Figure 4.1j,k,l), ($p<0.001$ for all regions). Interestingly, ripples in the hippocampus and temporal cortex seem to occur at opposed phase states of the ongoing delta oscillations. The ripples at frontal cortex occurred at preferred delta phases but with some participants locking to phases similar to the hippocampus ripples and others to the temporal cortex ripples (Figure 4.2).

4.4.2 Ripple-induced power modulation of cortical LFP

A widely accepted view, supported by a plethora of empirical research using single items as to-be-remembered material is that the formation of episodic memories relies on the coordinated activity of the hippocampal and cortical structures (Moscovitch et al. 2005; Yassa and Reagh 2013). Here we aimed at investigating the extent to which this crosstalk occurred during movie viewing on the bases of ripple-based activity. Indeed, hippocampal ripples are thought to be optimal for inducing synaptic plasticity (Buzsáki 2015; Sadowski, Jones, and Mellor 2016) and so the hippocampus could potentially modulate neural activity through excitation or inhibition of a wide range brain regions during ripple occurrence (Logothetis et al. 2012; Kaplan et al. 2016). To examine for the possibility of ripple-triggered changes in the ongoing activity at the neocortex during the encoding of a movie, we looked at LFP power changes in frontal and temporal cortical regions locked to hippocampal ripple occurrence. Additionally, we investigated the potential for neocortical regions to initiate ripples that subsequently influenced the ongoing activity in the hippocampus. This observation would indicate the involvement of feedback-based coordination, suggesting a reciprocal interaction between neocortical and hippocampal regions in the occurrence of ripples.

Our analysis revealed a decrease of LFP power in the hippocampus at high frequencies (>13Hz)

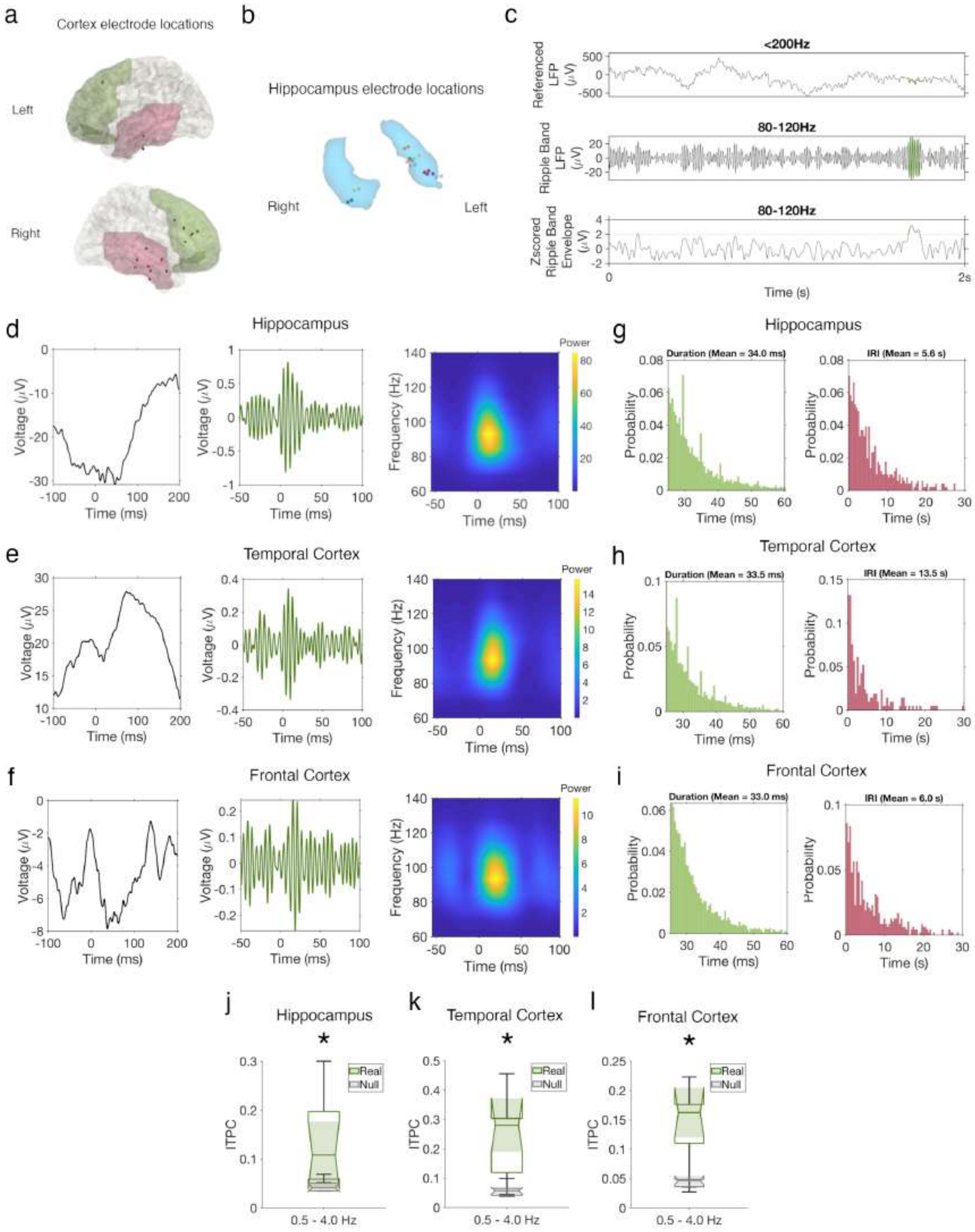


Figure 4.1: a) Temporal cortex (red) and frontal cortex (green) electrode localizations from all the participants mapped into common space, shown on a three-dimensional model. b) Hippocampal electrode locations, each color representing one participant. Each pair of dots indicates the two electrodes from the participants used for bipolar referencing, resulting in one trace per patient. b) Color-coded temporal order distribution of movie events that were recalled in the free recall task for each participant. c) Example of procedure for identifying ripples. Top to bottom: raw LFP; LFP filtered in the 80–120 Hz ripple band; envelope of the ripple-band LFP. In green an example of an identified ripple. d) Grand-average voltage trace of hippocampal ripples across all channels in the LFP (<200Hz) time domain, filtered in the ripple band (80-120Hz) (middle) and their power spectrogram in the time-frequency domain (right), e) similarly for temporal cortex and f) frontal cortex. g) Distribution of ripple durations (green) and inter-ripple intervals (IRIs) (red), across all participants for hippocampus, h) similarly for temporal cortex and i) and frontal cortex. j) Inter-trial phase coherence (ITPC) values across ripples (green) and surrogate data (gray), for hippocampus, k) similarly for temporal cortex and l) frontal cortex. * Significant at group level ($p < 0.05$).

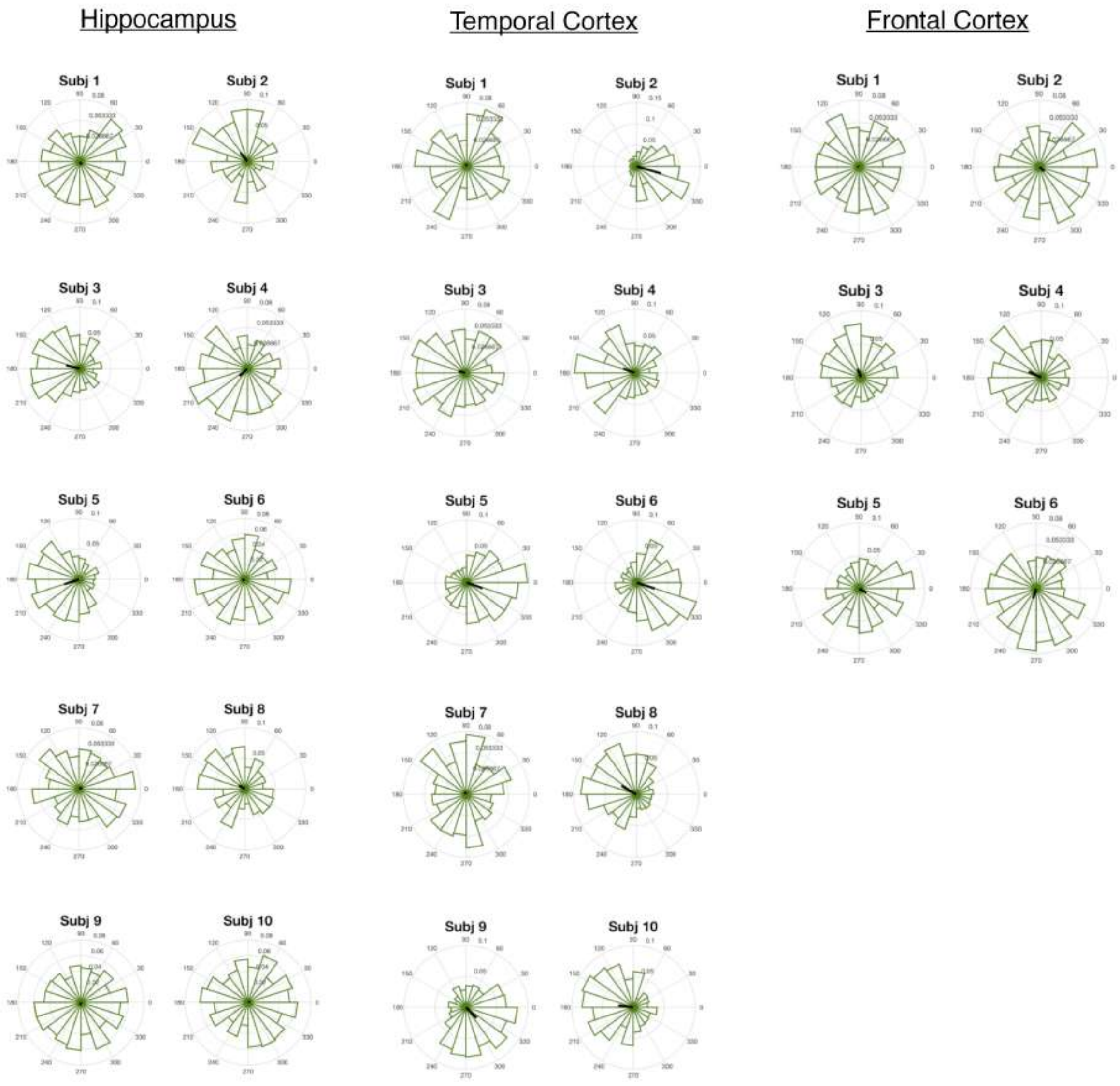


Figure 4.2: Polar distribution of delta phase angles at the onset of the a) hippocampal, b) temporal cortex and c) frontal cortex ripples, for each participant. Grand average across ripples is depicted by the thick red line.

during temporal cortex ripples (cluster permutation test, tmax = -2.26, tsum = -73653, $p < 0.001$; Figure 4.3a). Conversely, we observed a decrease of LFP power in the temporal cortex at low frequencies (<13Hz) around hippocampal ripples (cluster permutation test, tmax = -2.26, tsum = -54401, $p < 0.001$; Figure 4.3b). Weaker effects, though in the same direction, were observed in the frontal cortex (cluster permutation test, tmax =-2.57, tsum = -9429.3.4, p = 0.002, Figure 4.3c; cluster permutation test, tmax = -2.57, tsum = -1385, p = 0.047, Figure 4.3d).

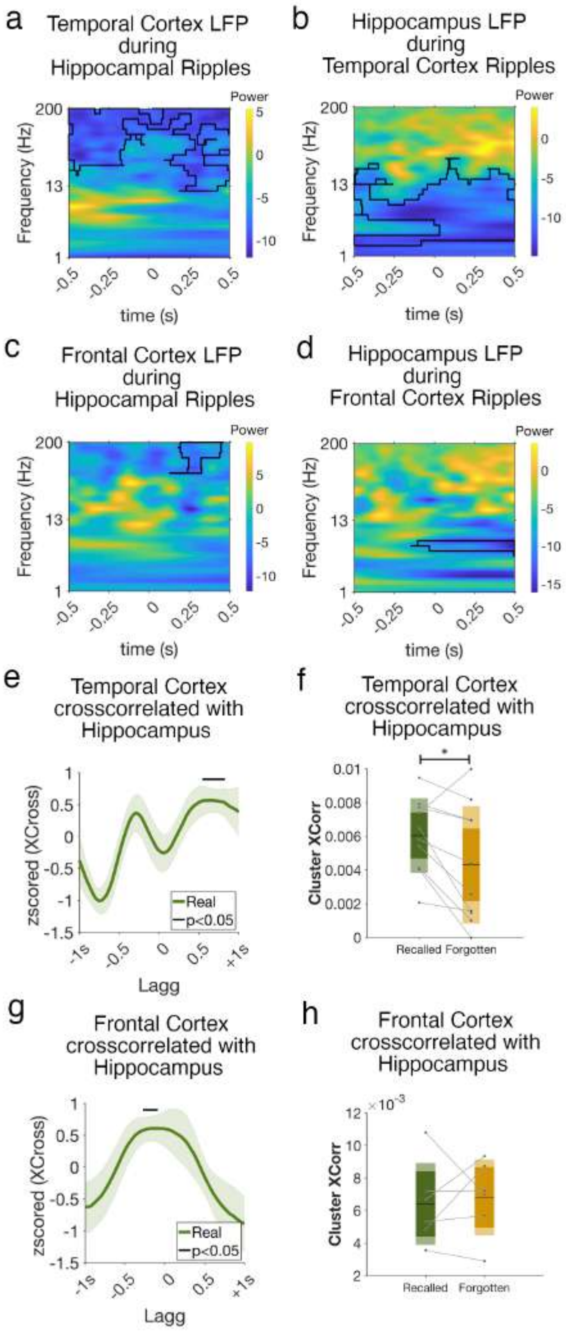


Figure 4.3: a) Time–frequency LFP power in temporal cortex during hippocampal ripples, where 0 corresponds to ripple peak. Black contours correspond to statistically significant clusters (two-sided cluster-based permutation tests: $p < 0.05$). b) Similar but for LFP power in the hippocampus during temporal cortex ripples. c) Time–frequency LFP power in frontal cortex during hippocampal ripples, where 0 corresponds to ripple peak. Black contours correspond to statistically significant clusters (two-sided cluster-based permutation tests: $p < 0.05$). d) Similar but for LFP power in the hippocampus during frontal cortex ripples. e) Cross-correlations between hippocampal and temporal cortex. Shaded region corresponds to SEM across participants. Black line at top indicates cross-correlations significantly above 0 (cluster-based permutation test: $p < 0.05$). f) Cross correlation values averaged across significant cluster identified in e) separated between ripples that occurred in events that were later remembered or forgotten. g) Cross-correlations between hippocampal and frontal cortex. Shaded region corresponds to SEM across participants. Black line at top indicates cross-correlations significantly above 0 (cluster-based permutation test: $p < 0.05$). h) Cross correlation values averaged across significant cluster identified in g) separated between ripples that occurred in events that were later remembered or forgotten. * Significant at group level ($p < 0.05$).

4.4.3 Ripple-based hippocampo–neocortical interaction and its impact on memory formation

Ripples have been shown and to co-occur between cortical areas and between the cortex and hippocampus during both spontaneous waking and NREM (Dickey et al. 2022; Verzhbinsky et al. 2023). To quantify the temporal relationship between ripple occurrence in the hippocampus and in the temporal and frontal cortex, we calculated a cross correlation between the ripple time series of both between these brain regions. Our analysis revealed a statistically significant peak of correlation, observed at approximately a 500ms time lag, when compared to surrogate data using a cluster permutation test (cluster permutation test, tmax = 2.93, tsum = 1587.4, $p < 0.001$). This finding provides evidence that temporal cortex ripples tend to occur before hippocampal events (Figure 4.3e). Conversely, our findings indicate that frontal cortex ripples tend to occur approximately 200ms after hippocampal events (cluster permutation test, tmax = 2.88, tsum = 1069.5, $p < 0.001$; Figure 4.3g). These results align with prior investigations demonstrating the temporal coupling between hippocampal ripples and ripples in various other brain regions (Axmacher, Elger, and Fell 2008; Vaz et al. 2019; Verzhbinsky et al. 2023; Dickey et al. 2022).

To investigate the potential involvement of ripple-based temporal coordination between hippocampal and neocortical regions in the formation of memories during movie viewing, we analyzed the ripples based on whether they occurred during events that would be remembered or events that would be forgotten. We then calculated cross-correlation values between the time series of the two regions, as we had done previously, separately for the time-series of ripples occurring during recalled events and the one of ripples occurring during forgotten events. By averaging the correlation values for the identified significant cluster, we observed that this temporal relationship at the temporal cortex only occurred for events that were later recalled (t(9)=2.56, p = 0.03; Figure 4.3f), while no difference was found at the frontal cortex (t(5)=-0.37, p=0.73) (Figure 4.3h).

Additionally, we sought to explore whether there might be a correlation not only between the temporal dynamics but also the frequency of ripples occurring within an event and the successful encoding of that event into memory. To address this issue, we compared the number of ripples, normalized by the length of each event, occurring within events that were remembered or forgotten and observed no differences for hippocampal events (t(9)=-0.66, p=0.53) or frontal cortex events (t(5)=0.28, p=0.79) but a clear difference at the temporal cortex in which remembered events tended to elicit more ripples in this region (t(9)=3.25, p=0.01; Figure 4.4). Together with the cross-correlation memory differences one could suggest that only those events that are relevant for consolidation are subsequently transferred to the hippocampus.

4.4.4 Hippocampal ripples increase around event boundaries

Boundaries are shifts in ongoing event models and are thought to be the moments in time when the organization and binding of information into long-term memory occurs (Ben-Yakov and Henson 2018; Baldassano et al. 2017; Silva, Baldassano, and Fuentemilla 2019). In line with the idea that hippocampal ripples promote memory formation for just encoded events in rodents (Foster and

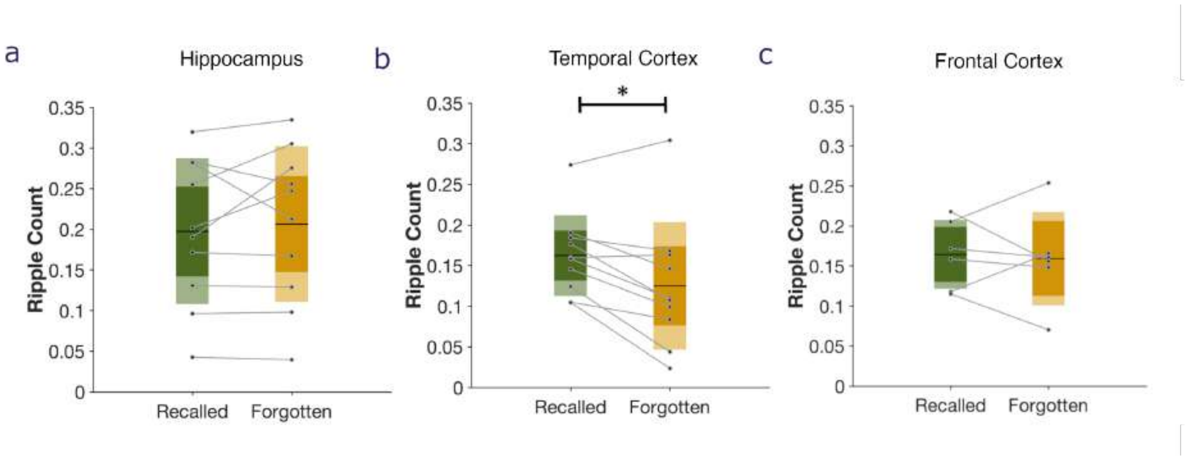


Figure 4.4: Average amount of ripples within an event, for each participant, normalized by the length of the event, for recalled (green) and forgotten (yellow) events, for a) hippocampus, b) temporal cortex and c) frontal cortex. * Significant at group level ($p < 0.05$).

Wilson 2006; Diba and Buzsáki 2007; Karlsson and Frank 2009), here we aimed at testing the hypothesis that hippocampal ripple occurrence would increase around event boundaries during movie viewing, akin to brief temporal opportunity windows of memory plasticity during awake encoding (Foster 2017). To test this hypothesis, we calculated a peri-boundary ripple rate by computing the peristimulus time histogram (PSTH) relative to all boundary onsets and compared it to a null distribution by shuffling the temporal order of the events while maintaining their lengths. We found that there was a marked increase in hippocampal ripple activity concomitant with a reduction in cortical electrode activity specifically at boundaries (Figure 4.5). It is noteworthy to mention that while the decline in the frontal cortex reached statistical significance, it did not withstand multiple comparison correction using the false discovery rate (FDR), potentially due to the relatively small sample size of participants in our study. The increase of hippocampal ripples at boundaries is in line with fMRI studies which show that stronger event encoding was related to a lower hippocampal activation during the event and a high activation at its offset (*i.e.*, at boundaries) (Ben-Yakov and Henson 2018; Baldassano et al. 2017). The decrease at the cortex could be indicative of a switching mechanism in which cortical regions need to be silenced at moments in which resources have to be concentrated at the hippocampus (Logothetis et al. 2012).

4.5 Discussion

Real life experiences entail an unbroken succession of interconnected information, linking each moment together. Nevertheless, the neural mechanisms underlying episodic memory formation amid the continuous fluctuations of stimuli remain elusive. In this study, we recorded intracranial electrophysiological data from patients to examine the properties and interactions of ripples in hippocampus and in frontal and temporal cortex while participants watched a movie. We found that ripples co-occur in the hippocampus and cortical areas during the encoding of an event and impact the LFP signal when a ripple occurs. This temporal dynamic has an impact in the memory encoding of an event, as ripples occurring in the temporal cortex correlate with later recollection of that event. Additionally, hippocampal ripple activity increased at event boundaries and within events at the cortical level,

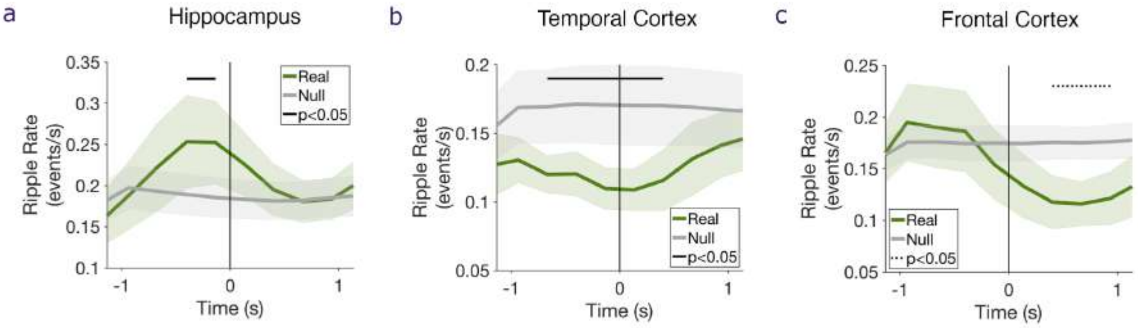


Figure 4.5: Instantaneous SWR rate computed in 300ms time bins around boundary onset and smoothed by a five-point triangular window, for empirical data (green) and surrogate data (grey), computed by shuffling the temporal order of the events while maintaining their lengths, for a) hippocampus, b) temporal cortex and c) frontal cortex. Shaded region corresponds to SEM across participants. Black line at top indicates significant clusters with FDR correction ($p < 0.05$) and black dashed line at top indicates significant clusters with no FDR correction ($p < 0.05$)

reflecting a distinctive recruitment of this type of activity. This cortico-hippocampal ripple-based communication during encoding highlights the involvement of ripples in the formation of episodic memories in naturalistic circumstances.

The interaction between the cortex and the hippocampus plays a pivotal role in the encoding of events. An accepted view is that the cortex processes and analyzes information related to an event and the hippocampus provides the temporal and contextual framework necessary for organizing and integrating the elements of an event into coherent event representations (Reagh and Ranganath 2023). The communication between these brain regions during event encoding ensures the integration of perceptual details with contextual information, facilitating the formation of meaningful and distinct memory traces. One mechanism through which the brain achieves this integration is through sharp wave-ripples. Ripples are not isolated hippocampal events but are part of a complex system of interconnected oscillatory networks involving the cortex and hippocampus (Dickey et al. 2022). The coordination of these networks facilitates specific information transfer between neocortical and hippocampal cell assemblies, contributing to the cohesive processing and encoding of event-related information.

In this study, we observed a pattern of ripple activity occurring in the temporal cortex preceding those in the hippocampus, particularly during events that were later successfully recalled. This finding aligns with models of hippocampo-cortical interactions in memory processing. For example, it parallels previous research indicating that hippocampal ripples tend to precede cortical ripples during sleep, while cortical ripples tend to precede hippocampal ripples during wakefulness (Dickey et al. 2022). The temporal cortex, particularly the anterior temporal lobe where the majority of electrodes used in this analysis were placed, plays a critical role in semantic memory and represents information about objects and individuals (Bonner and Price 2013; Reagh and Ranganath 2023). The observed precedence of ripple activity in the temporal cortex suggests its involvement in capturing this type of information and subsequent transmission to the hippocampus. The hippocampus, known for its role in incorporating event-specific details into comprehensive memory traces, receives the information from the temporal cortex and integrates it into a complete description of the event. During the event encoding process, cortical ripples may then be triggered by stimulus-specific neuronal activity, facilitating the transfer of information from extrahippocampal regions to the hippocampus. This dynamic interplay between the temporal cortex and the hippocampus during event encoding highlights the collaborative nature of memory formation and the distinct contributions of these regions in processing and consolidating event-related information.

In contrast, we observed that ripples in the hippocampus preceded those in the frontal cortex electrodes, consistent with previous findings demonstrating that activity in frontal areas precedes hippocampal ripples (Logothetis et al. 2012; Jadhav et al. 2016). The frontal cortex receives direct and indirect projections from the hippocampus (Cenquizca and Swanson 2007) and has been implicated in various functions such as decision-making, long-term memory consolidation, and working memory (Cenquizca and Swanson 2007). The majority of frontal electrodes included in this analysis were located in rostral areas, which have also been associated with prospective memory (Volle et al. 2011). Although the precise role of the frontal cortex in the current task remains uncertain, it seems reasonable to us to hypothesize its involvement in monitoring working memory maintenance during an event (Kurby and Zacks 2008; Radvansky 2017). The temporal dynamics of ripple coupling between the frontal cortex and hippocampus was not associated to whether an event would be later recalled or forgotten. This suggests that ripples in the frontal cortex may not necessarily be encoding specific event details. Instead, they could potentially serve as a mechanism for detecting transient changes in the event, much like a working memory maintenance mechanism, allowing the brain to update event models and respond accordingly.

Similar to recent research on human hippocampal ripples (Axmacher, Elger, and Fell 2008; Kunz et al. 2022), we found that ripples occurred in a phase-locked manner to specific phases of delta band activity. Neocortical delta oscillations have been associated with alternating states of enhanced and reduced cortical excitability, known as up and down-states (Steriade, Nunez, and Amzica 1993). Studies in rats have revealed that hippocampal ripples were synchronized with the depolarizing phase of neocortical delta waves and were more likely to occur during down-states than during up-states, often coinciding with transitions from down to up-states (Battaglia, Sutherland, and McNaughton 2004). While most of these studies have been conducted during sleep, an interesting hypothesis to investigate in future studies would be to explore the possible association of ripple activity with up and down-state during awake time.

We also observed widespread changes in LFP that were linked to the occurrence of ripples. When a ripple occurred in the hippocampus, cortical high-frequency activity was suppressed, and conversely, when a ripple occurred in cortical areas, hippocampal activity showed an opposite suppression pattern. Furthermore, these observations, combined with the fact that ripples in the hippocampus and cortical areas appeared to be locked to opposite phases of the delta band, suggest the existence of a dynamic system where the occurrence of ripples during specific transitions from down to up-states may influence the silencing or activation of specific brain areas.

The hippocampus has been found to exhibit heightened activity and engagement at event boundaries (Ben-Yakov, Eshel, and Dudai 2013; Baldassano et al. 2017; Ben-Yakov and Henson 2018), while other cortical areas appear to be more sensitive to representing information within an event (Reagh and Ranganath 2023). In our study, we observed that this alternating recruitment pattern during the encoding of an event is reflected at the level of ripple occurrence. Specifically, when examining event boundaries, we observed an increase in hippocampal ripples accompanied by a decrease in cortical ripples. These findings, along with the previously mentioned results, underscore how the complementary functions of different cortico-hippocampal networks enable the brain to flexibly construct and reuse mental representations of event components. The recruitment of ripples at different moments and in different areas during the encoding of a dynamic event may serve as a computationally efficient strategy for simplifying complex events into key components. Furthermore, the coactivation of stimulus-specific cells during hippocampal ripples, as observed during the encoding of object-place associations in humans (Kunz et al. 2022), suggests that ripples may play a facilitative role in binding diverse memory elements represented across distinct cortical areas. This facilitation enables the formation of coherent event representations, supporting the integration of information from different cortical regions.

The investigation of ripple events during awake behavior in rodents has uncovered a structured and temporally compressed replay of hippocampal multicell sequences representing past navigation-related experiences, as well as "preplay" of potential future (Diba and Buzsáki 2007; Pfeiffer and Foster 2013; Jadhav et al. 2012; Foster and Wilson 2006; Gupta et al. 2010). Boundaries, have been shown to trigger a rapid reinstatement of the just encoded event, facilitating its consolidation into long-term memory (Sols et al. 2017; Silva, Baldassano, and Fuentemilla 2019; Xu et al. 2019). The relationship between the observed increase in ripples at boundaries and this post-boundary reinstatement pattern remains unknown. Further research is needed to determine whether there is a connection between these two boundary phenomena and whether there is any link between the occurrence of ripples throughout event encoding and replay. Investigating these aspects will shed light on the mechanisms underlying memory consolidation and the role of ripples in the dynamic interplay between hippocampal activity, event boundaries, and replay processes.

In sum, our findings suggest that ripples could be involved in the binding of memory elements represented across disparate cortical areas into coherent representations. Additionally, we observed increased ripple activity at event boundaries in the hippocampus and within events in cortical regions, reflecting the distinctive patterns of information processing during different temporal periods. These findings shed light on the intricate mechanisms underlying memory encoding and provide insights into the role of ripples in event segmentation and memory consolidation.

Chapter 5

Study 3: Rapid brain signaling of hierarchical relational knowledge in goal directed behavior

5.1 Summary

This study goal was to investigate the role of boundaries in organizing the state-space into a hierarchical map representation and their influence on goal-directed behavior. Drawing on modular network environments, where interconnected nodes operate collectively, the study explores the impact of detecting event boundaries on optimal goal-directed behavior. While acquiring scalp EEG data, participants had to navigate fractal picture sequences to find optimal paths for rewards. Using linear discriminant analysis, we examined how the acquisition of hierarchical event memory representations within and between communities get represented in the brain and influence decision-making. Our results sheds light on the cognitive mechanisms underlying goal-directed behavior and contribute to our understanding of how individuals organize knowledge in complex environments.

5.2 Introduction

Understanding the neural mechanisms underlying learning is a fundamental pursuit in cognitive neuroscience. In recent years, there has been a growing interest in investigating learning within modular network environments, characterized by interconnected components or modules that operate collectively to accomplish complex cognitive tasks (Schapiro et al. 2013; Lynn and Bassett 2020; Mark et al. 2020). Modular networks provide a unique and ecologically valid framework for studying learning, as they closely resemble real-world scenarios where information is organized into distinct functional units or events (Karuza, Thompson-Schill, and Bassett 2016). But how do we acquire the understanding that sequences of elements in our environment are organized into separate and distinct events?

Growing evidence suggests that learners possess a sensitivity to the network properties present in their environment, spanning various domains. For instance, studies have demonstrated that the clustering coefficient of a word, which indicates the degree of relatedness between its phonological neighbours, can predict the word's acquisition success (Goldstein and Vitevitch 2014). Beyond language, adults have shown the ability to utilize higher-order temporal relations to segment visual events from continuous image streams. In previous research (Schapiro et al. 2013), participants were exposed to a sequence of images generated through a random walk on a network comprising densely interconnected nodes grouped into communities (like in Figure 5.1a). In this sequential scenario, nodes belonging to the same cluster or community display temporal associations that overlap, as they tend to be preceded and followed by sets of nodes belonging to the same cluster. In contrast, nodes from different clusters exhibit less temporal overlap in their associations. This characteristic pattern of temporal overlap provides a potential foundation for how sequences of stimuli get divided into discrete events, even when the transition probabilities between nodes are uniform. Notably, strong modular structure has been shown to help people build more accurate mental representations of a network, thereby allowing humans to better anticipate future items and events (Schapiro et al. 2013; Karuza, Thompson-Schill, and Bassett 2016; Karuza et al. 2017; Kahn et al. 2018; Lynn and Bassett 2020), which is a guiding principle for optimal decision-making in complex environments. Nevertheless, how goal-directed behavior is influenced by how sequences of elements get structured into a hidden modular structure still remains to be explored.

Here, we draw on previous modular graph structure task designs (*e.g.*, Schapiro et al. 2013; Kahn et al. 2018; Lynn and Bassett 2020) to investigate how the detection of event boundaries in the network fosters optimal goal-directed behavior. We aimed at examining how the acquisition of such topology structure can lead to the discovery of hierarchical representations hidden in a relational structure. We recorded scalp EEG while participants were asked to find out optimal paths that linked sequences of fractal pictures to a reward. Critically, picture sequences and paths coalesced around clusters or 'communities' of mutually predicting stimuli, thereby eliciting the emergence of hierarchical event memory representations for picture images, those that linked within and those that linked between (*i.e.*, boundaries) communities (Figure 5.1a). In our work, we followed previous proposals (Schapiro et al. 2013) that showed that stimuli with similar temporal contexts were grouped together in a representational space, forming clusters that facilitated the discrimination of events. This idea parallels theories of event segmentation in memory studies, in which the continuous stream of information is discretized into separate episodic memories (Zacks et al. 2007). In both cases, the structure of events relies on the clustering of representations in an internal space. Items within the same event are represented similarly to each other and dissimilar to other items (Ezzyat and Davachi 2014). Given that decision-making processes in complex environments are enhanced by the rapid access of a structured representation of the underlying relationships between elements, we hypothesized that the use of such community or event structure representational space would be activated very rapidly, at early stages of the encoding of an item. Additionally, we also searched the possibility that the different items within a network could in fact encompass representations that demonstrate increasing complexity, specifically the simultaneous tracking of community structure alongside boundary and non-boundary representations. Finally, we explored the extent to which the acquisition of such structural representation in one day (Day 1) may be transferred to a novel task the day after (Day 2) that shared similar graph structure but differ in their items.

5.3 Materials and Methods

5.3.1 Participant Sample

Thirty participants (28 right-handed, 16 females, age range 18 – 38 years, mean = 25.6 years) participated for pay (10€/h) and were recruited from the University of Barcelona and the broader community. All participants were healthy and did not consume psychoactive substances. Informed consent was obtained from participants in accordance with procedures approved by the Ethics Committee of the University of Barcelona. Data from 2 participants were discarded after verifying that their performance was below 2SD of the mean. Thus, the final sample of participants included in the study was 28.

5.3.2 Experimental Design and Stimuli

An experimental design based on the one applied in Schapiro et al. 2013a was implemented on PsychoPy (Peirce et al. 2019). The stimuli consisted of two set of 12 abstract images created in ArtMatic Pro (http://www.artmatic.com/) organized in a graph structure of equally distant nodes (Figure 5.1a). Participants were required to form a mental representation of the relative distance between the series of images that were connected in the map. The task implied that they had to learn and find the optimal paths that linked the sequences which allowed them to reach a goal. Unbeknown to the participant, these picture sequences and paths formed clusters or 'communities' of mutually predicting stimuli, thereby eliciting the emergence of hierarchical event memory representations. Critically, only a sub-sample of the items within the community were linked to items from other communities allowing the transition between clusters, which we will here on by describe as boundaries (Figure 5.1a), and the other sub-sample only allowed within community transitions, which we will describe as non-boundaries (Figure 5.1a).

Participants were instructed that on every trial they would have to select between a set of images until they found a goal image. On each trial, before having to make a choice, participants were cued with the goal image and with the three images from which they would have to choose from, each for 1500 ms interleaved by 600 ms of a fixation cross (Figure 5.1b). This allowed us to study the brain response to each item individually while avoiding the active choice moment and the noise associated to the button press. They would begin each trial with a total of 12 points and their goal would be to find the goal image as fast as possible and without losing points. Points were kept if the participant selected a correct image, and 1 point was lost if the participant selected a wrong one. We computed correct responses when the selected image brought them closer to the goal or kept them at the same distance as they were before. Wrong selections were computed if the selected image left them further away from the goal.

The experiment was formed by a total of 42 trials of two types. In the first type, participants had to complete a set of trials where both the starting point and the goal were non-boundary items belonging to different clusters. For all the combinations participants were required to take at least

3 steps until they found the goal (Figure 5.1c). For the second type, participants had to go from a boundary item to another boundary item, either belonging to a different or to the same cluster. For these combinations' participants were required to take at least 3 (across communities) or 2 (within community) steps until they found the goal (Figure 5.1c). The trials were organized in the following blocks: 12 trials of non-boundary to non-boundary sequences, 6 trials of boundary to boundary across clusters sequences, 12 trials of non-boundary to non-boundary sequences and 12 trials of boundary to boundary for both across and within sequences interleaved in sets of 3 trials. The trials were randomized within each block for each participant. The experiment can then be divided in two parts, both containing a set of non-boundary to non-boundary and boundary to boundary trials. Crucially both parts contained the same sequences of items but in the second part the opposite direction was tested (the starting points of the first half would be tested has the goal on the second part and the goals of the first half would be tested as starting points on the second half of the experiment) which ensured that participants were never required to perform the same directional path.

5.3.3 EEG Recording and Preprocessing

EEG was recorded with a 64-channel system at a sampling rate of 512 Hz, using an eego amplifier and Ag/AgCl electrodes mounted in an electrocap (ANT neuro) located at 59 standard positions ((Fp1/2, AF3/4, Fz, F7/8, F5/6, F3/4, F1/2, FCz, FT7/8, FC5/6, FC3/4, FC1/2, Cz, T7/8, C5/C6, C3/4, C1/2, CPz, TP7/8, CP5/6, CP3/4, CP1/2, Pz, P7/8, P5/6, P3/4, P2/1, POz, PO7/8, PO5/6, PO3/4, Oz, O1/2) and at the left and right mastoids. Horizontal and vertical eye movements were monitored with electrodes placed at the right temple and the infraorbital ridge of the right eye. Electrode impedances were kept below 10 kΩ during the recording. The signal was then re-referenced to the linked mastoids, bad channels were interpolated, and a band-pass filter (0.1 Hz - 30 Hz) was implemented offline. Blinks and eye movement artifacts were removed with independent component analysis (ICA) before the analysis.

The continuous EEG data was then epoched into 1500 ms segments (relative to trial onset) corresponding to the visualization of the goal and option items prior to being asked to take a decision, and a pre-stimulus interval of 100 ms was used as the baseline for baseline correction procedure. Trials exceeding $\pm$ 100μV in EEG and/or EOG channels were rejected offline. Trials containing noise not detected through the later methods were rejected after visual inspection. The data segments were then normalized by z-scoring all time points so that the mean of every electrode was 0 across time, smoothed with a gaussian kernel with bandwidth of 80 timepoints and downsampled by a factor of 5, which resulted in final segments of 1300 ms which were used for the later analysis.

5.3.4 Behavioural Data Analysis

We used the number of steps taken to reach the goal to assess participants performance. We expected this value to reduce if participants learned how to reach the goal faster and in a most direct way. To do this we divided the experiment in two halves (as explained in the experimental design section) and compared the average number of steps of each participant between the two using a

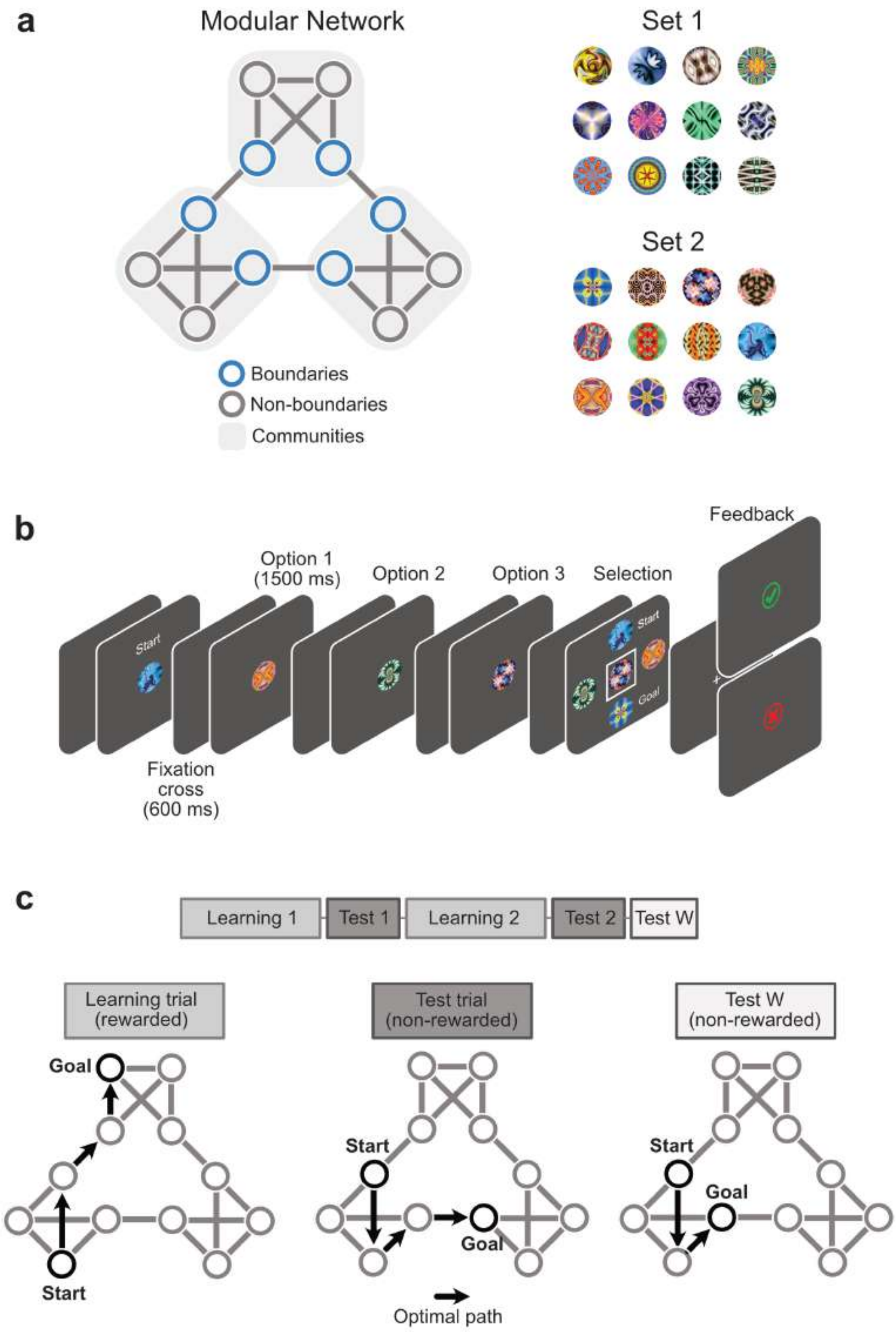


Figure 5.1: Task Design and trial structure. a) Representation of the graph structure underlying sequences in the experiment. The graph consisted of three distinct communities of interconnected nodes. Each node in the graph corresponded to a unique fractal image, and edges between nodes corresponded to their possible co-occurrence in a sequence. Sets of fractal image stimuli used in the two versions of the graphs in the study are displayed on the right. b) Trial presentation scheme. (c) Structure of the task and the optimal trajectory in each trial during the Learning and type of Test phase.

paired student t-test. We performed this analysis excluding the trials where both the starting point and goal were boundary items belonging to the same cluster given that this type of trials were only performed during the second half of the experiment and the optimal number of steps between the two is smaller than the other conditions.

Additionally, we aimed to examine whether participants tended to select more boundary items over time. This was based on the observation that, for most start/goal pairs, opting for boundary items would lead to a more optimal path towards the goal. To investigate this, we calculated a percentage by dividing the number of chosen boundary items by the total number of selected items in each trial. Subsequently, we averaged this percentage for each participant across the two halves of the experiment. To compare the two halves, we employed a paired student t-test.

5.3.5 Linear Discriminant Analysis (LDA)

A linear discriminant analysis (LDA) was used to classify the hierarchical features of the map (each cluster community vs the others and boundaries vs non-boundaries) based on the EEG topography at a given time point. The classifier was trained and tested on the 1300 ms signal amplitude epochs of the 59 electrodes, corresponding to the item presentation prior to choice, resulting in a single decoding time course by using functions from the MVPA-light toolbox (https://github.com/treder/MVPA-Light). During training, an estimation of whether the unlabelled pattern of brain activity belonged to each class was made based on the computation of a decision boundary that best separated the different classes in a high-dimensional space. This final decoding time course would then indicate how confident the classifier was at assigning a given item to a given category. The LDA was trained and tested independently per participant at each time point using a leave-one-out cross-validation approach, first assuming two different classes (*i.e.*, if an item was a boundary or a non-boundary) and then assuming three classes (*i.e.*, to which of the three clusters it belonged to).

We used a permutation test (Groppe, Urbach, and Kutas 2011) to deal with the multiple comparisons problem given the 138 temporal points, covering the 0 to 1300 ms epoch length, included in the analysis. This test uses the “tmax” method for adjusting the p-values of each variable for multiple comparisons (Blair and Karniski 1993). Like Bonferroni correction, this method adjusts p-values in a way that controls the family-wise error rate.

Note that for all the LDA analyses in this study, the training set and test set for each participant were z-transformed for each channel and each timepoint across all the trials before the application of LDA.

5.4 Results

5.4.1 Behavioural results

We first evaluated behaviourally if participants were performing better with time and if there was any evidence that they were learning the structure of the map. Participants improved during the task as they relied on less number of movements to reach the goal in the second half (M = 7.27; SEM = 2.71) than in the first half of the task (M = 8.51; SEM = 2.66) (paired ttest; t(27) = 2.73, p = 0.01) (Figure 5.2a). We also found that, on average, participants selected more boundary than non-boundary items in trials in both learning phases (t(27) = 12.32, $p < 0.01$), but that the greater proportion of boundary item selection was similar in the two learning phases (t(27) = -1.23, p = 0.22) (Figure 5.2b).

A regression model implemented at individual level confirmed that the greater the number of times participants selected boundary items in a trial was associated to lesser number of movements in that trial (t(27) = -9.63, $p < 0.001$) and to greater amount of budget received (t(27) = 9.49, $p < 0.001$), thereby indicating that participants learned that selecting boundaries was an optimal behaviour in the task.

We next sought to assess whether participants showed improved behaviour between the first test(just after the 1st learning phase) and the second test (just after the 2nd learning phase) in the task (Figure 5.2a). The extent to which participants showed behavioural improvement in these tests was critical to conclude that they were learning the representation structure of the network as their behaviour was not rewarded in these tests. First, we found that, on average, participants required lesser number of movements to reach the goal in the 2nd than in the 1st test (paired ttest: t(27) = 9.68, $p < 0.001$). We also found that participants selected more boundary items than non-boundary items in the 2nd than in the 1st test (t(27) = 3.16, $p < 0.004$). Finally, we observed a significant difference in participants' performance between the final test Within condition and test 2. Specifically, participants exhibited a notable decrease in the number of moves required to reach the goal in test Within compared to test 2, indicating a higher efficiency in navigating the task (t(27) = 5.27, $p < 0.001$) (Figure 5.2a).

In summary, the findings on Day 1 suggest that participants gradually incorporate the hidden community path structure connecting items, recognizing the presence of distinct item types (boundaries and non-boundaries) within the hierarchical representation. By selecting boundary items, participants move closer to their objective as they enable a transition to a different community.

On Day 2, we replicated the findings from Day 1. Participants improved during the task as they relied on less number of movements to reach the goal in the second (M = 6.58; SEM = 1.84) than in the first half of the task (M = 7.06; SEM = 1.66) (paired ttest; t(27) = 2.21, p = 0.035) (Figure 5.2c). As in Day 1, they were also more prompted to select more often boundaries than non-boundary items during the task (t(27) = 13.39, $p < 0.01$) and that the proportion of boundaries selected per trial was similar in the 1st and in the 2nd half of the learning task (t(27) = -1.18, p = 0.25) (Figure 5.2d). We also assessed whether participants showed improved behaviour between the first and the

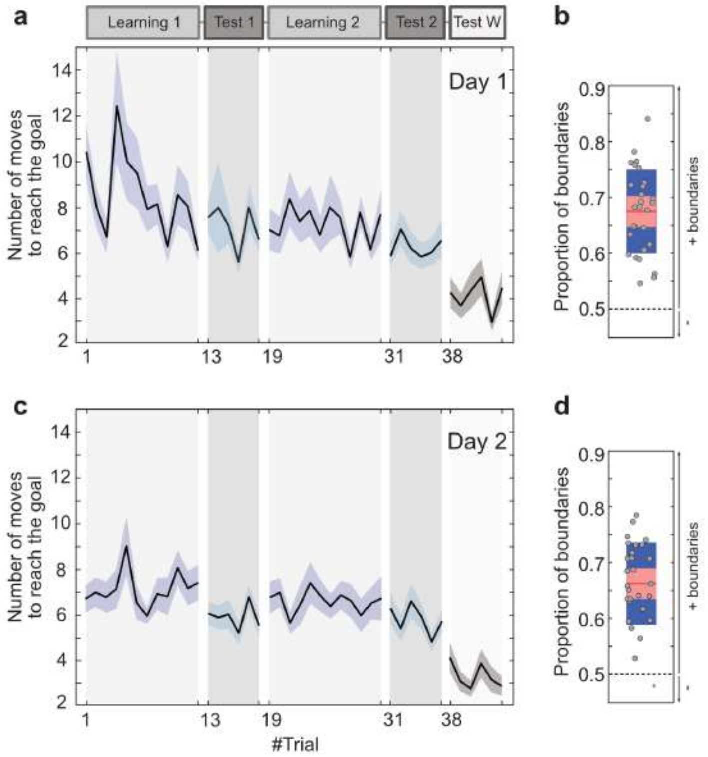


Figure 5.2: Behavioural results. a) Number of moves (steps) at each trial throughout the experiment. Thick line represents mean across participants and shades represents the standard deviation of the mean. b) Boxplot with average number of steps per participant for the 1st and 2nd half of the experiment.

second test. However, contrary to data in Day 1, participants did not show a reduction of number of moves on test 2 when compared to test 1 (paired ttest: t(27) = 0.40, p = 0.69). Finally, we again found that participants were more rapid in finding the goal in the final test Within compared to test 2 (t(27) 6.56, $p < 0.001$) (Figure 5.2d).

As in Day 1, a regression model implemented at individual level confirmed that the greater the number of times participants selected boundary items in a trial was associated to lesser number of movements in that trial (t(27) = -7.04, $p < 0.001$) and to greater amount of budget received (t(27) = 7.33, $p < 0.001$), thereby indicating that participants learned that selecting boundaries was an optimal behaviour in the task.

5.4.2 Rapid brain signalling of the modular structure during the task

Our initial objective was to investigate whether participants' brain activity reflected the emergence of fundamental properties of modular structure in the encoding of task-related items, specifically the differentiation between boundary and non-boundary items, as well as the representation of community structure among the elements.

We utilized an LDA to investigate whether EEG activity patterns evoked during image presentation could differentiate between images that served as boundaries and images that were included in the network as non-boundaries. We conducted this analysis separately for EEG signals recorded from anterior and posterior scalp electrodes on both Day 1 and Day 2. The analysis revealed that participants were able to distinguish between boundary and non-boundary items with above chance accuracy, already at around 150-200 ms after image onset. While this discrimination was evident in the EEG signals recorded from both anterior and posterior scalp regions (Figure 5.3a), the LDA accuracy was much higher in the EEG signals from posterior scalp electrodes compared to the anterior ones and these findings were consistent across both Day 1 and Day 2 of the study (Figure 5.2a). These findings suggest that participants successfully acquired representations of both boundary and non-boundary items during the task and that these representations were not confined to specific brain regions but were distributed across the entire brain.

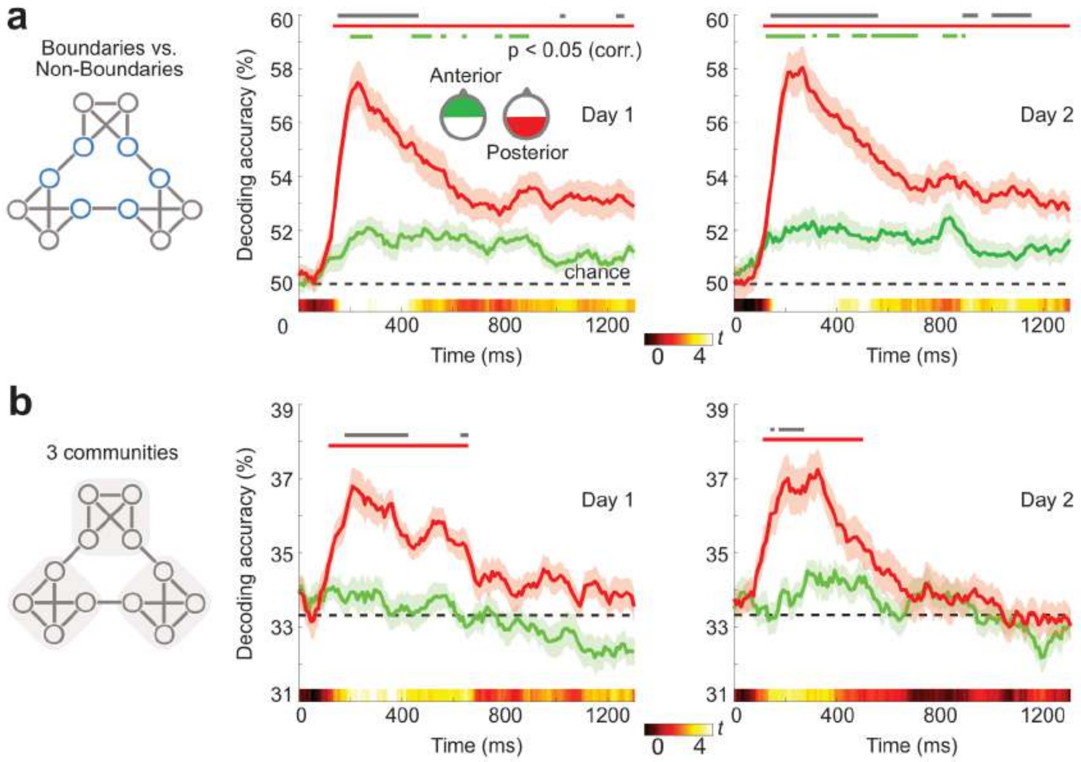


Figure 5.3: Temporal dynamics of EEG-based decoding accuracy using LDA. a) Point-to-point average LDA accuracy for Day 1 and Day 2 separately, considering the anterior and posterior scalp EEG electrodes. The discrimination task focuses on differentiating items that occupy a boundary and non-boundary position within the network, while keeping the participants blind to the stimuli. b) A similar figure structure is presented, highlighting the decoding accuracy in relation to the community structure of the items. Both (a) and (b) feature horizontal bars at the top, indicating time points where the classifier accuracy was statistically significant above chance level. For (a), chance level is set at 50%, while for (b), it is set at 33.3%. The color scheme distinguishes significance for frontal regions (represented by green bars) and posterior scalp regions (represented by red bars). Additionally, a grey bar signifies point-to-point statistical significance ($p < 0.05$, corrected) when comparing the decoding accuracy between the anterior and posterior regions. The thick line represents the averaged accuracy across participants, while the shaded area indicates the standard error of the mean (SEM) across participants.

Next, we investigated the potential of EEG signals to detect the acquisition of neural representations linked to community structure. To assess for this possibility, we trained separate LDAs using EEG data from anterior and posterior scalp regions for each experimental day, aiming to differentiate between images belonging to different communities. The results of this analysis revealed that the EEG signals successfully capture the representation of community structure, evident at a rapid latency of 120 ms from image onset (Figure 5.3b). However, in contrast to the previous findings indicating widespread distribution of boundary and non-boundary category representations throughout the brain, the representation of community structure was predominantly observed in the posterior scalp regions rather than the anterior scalp regions in both days (Figure 5.3b).

The differential findings between anterior and posterior brain regions in our study may be indicative of distinct neural processes and functional specialization within these regions, suggesting that the acquisition and representation of community structure and boundary and non-boundary distinction within a modular network may rely on neural mechanisms that are specific to the posterior scalp regions.

5.4.3 Capturing hierarchical relation between network items in posterior scalp region

A pressure question is the extent to which neurophysiological signals from posterior regions encompass representations that demonstrate increasing complexity, specifically the simultaneous tracking of community structure alongside boundary and non-boundary representations. If confirmed, these findings would provide valuable evidence supporting the brain's ability to form and utilize cognitive maps across various hierarchical dimensions, ranging from boundary and non-boundary elements within a modular network to the integration of community and boundary-level representations within a network.

To examine this issue, we employed separate classifiers trained and tested on data acquired from the posterior scalp EEG region. The objective was to distinguish community modules within the network based solely on the presence or absence of boundary items. Our findings demonstrated that EEG activity during the encoding of both boundary and non-boundary items successfully discriminated network communities. Importantly, the classification accuracy remained statistically similar when the classifier was trained and tested on data associated with boundary and non-boundary items, particularly on Day 1 (Figure 5.4a). However, while the classifier accuracy remained high for both boundary and non-boundary items on Day 2, we observed a higher accuracy for boundary items compared to non-boundary items (Figure 5.4a).

We observed inter-individual variability among participants in terms of performance improvement on Day 2 (Figure 5.4b). While some participants showed a substantial decrease in the averaged total number of moves during Day 2 in respect to Day, others did not show any change and even a small increase of the average number of moves in Day 2 compared to Day 1. We used a median split approach by divide the sample according to the degree of task improvement from Day 1 to Day 2. This way, we created a subsample of participants who showed little or no reduction of number of movements in Day 2 (*i.e.*, 'non-improvers', N = 12) and another subgroup of participants that showed a large decrease of number of moves in Day 2 (*i.e.*, 'improvers', N = 12) (Figure 5.4b).

Notably, the two groups exhibited a significant difference in terms of improvement measured by the number of moves (two-sample t-test: $t(22) = 7.83$, $p < 0.001$). However, both groups had a similar overall tendency to select a higher proportion of boundary items compared to non-boundary items on both Day 1 ($t(22) = 1.68$, $p = 0.11$) and Day 2 ($t(22) = -0.03$, $p = 0.97$). These results indicate that the degree of improvement between the two days cannot be solely attributed to a general increase in selecting boundary items during the task, but rather to an overall improved selection of items while navigating the map.

Given that the two groups of participants differed in their ability to navigate throughout the network in Day 2 in respect to Day 1, we reasoned that a plausible hypothesis would be that those who improved on Day 2 were capable to integrate better the hierarchical structure of the network and that this may be reflected in the degree of accuracy of the classifier to discriminate between communities as a function of whether they were better represented by the boundary or the non-boundary items. The results of this analysis showed that on Day 1, the temporally evolving accuracy of the classifier for both the ‘improvers’ and the ‘non-improvers’ was similar for boundary and non-boundary EEG elicited activity (Figure 5.4c). However, on Day 2, we found that the ‘improvers’, who showed a substantial decreased number of moves throughout the task compared to Day 1, showed greater accuracy in discriminating between network communities from EEG activity elicited from boundary than non-boundary items at $\sim$300-600 ms and at $\sim$900-1300 ms, being the latter time window effect surviving when statistical threshold was corrected for multiple comparisons ($p < 0.05$, corrected at cluster level) (Figure 5.4c). These results were confirmed with a repeated measures ANOVA (type of item x day interaction: $F(1,11) = 9.20$; $p = 0.01$).

5.5 Discussion

This study investigates the neural mechanisms underlying goal-directed behavior in a 2-day community network task environment. In the task, picture sequences and paths are organized into clusters or ”communities” of mutually predictive stimuli, giving rise to hierarchical event memory representations (Schapiro et al. 2013; Schapiro et al. 2016; Mark et al. 2020; Garvert, Dolan, and Behrens 2017). Contrary to previous research, where participants simply performed a random walk of the map, here participants had to learn the statistical regularities while being instructed to find specific images from the map. In this case, as every transition that occurs is equally likely, the moments of uncertainty or surprise arise from the choices taken to reach a goal and if a certain move was rewarding or not. Surprisingly, and even though they needed to engage in highly adaptative goal-directed behavior, as the goal changed on every trial, participants were able to learn the structure of the map and improve their performance from early on. We found that participants successfully detected item boundaries within the network, which was associated with fewer moves required to reach a goal.

Using scalp EEG recordings in combination with a time-resolved decoding approach, we observed that participants’ brain activity rapidly signaled the detection of both boundary and non-boundary items in the network, occurring at approximately $\sim$140 ms from stimulus onset. Notably, this discriminatory pattern of brain response was observed in both anterior and posterior scalp regions. However, only the posterior regions exhibited signals indicative of increasing complexity, representing

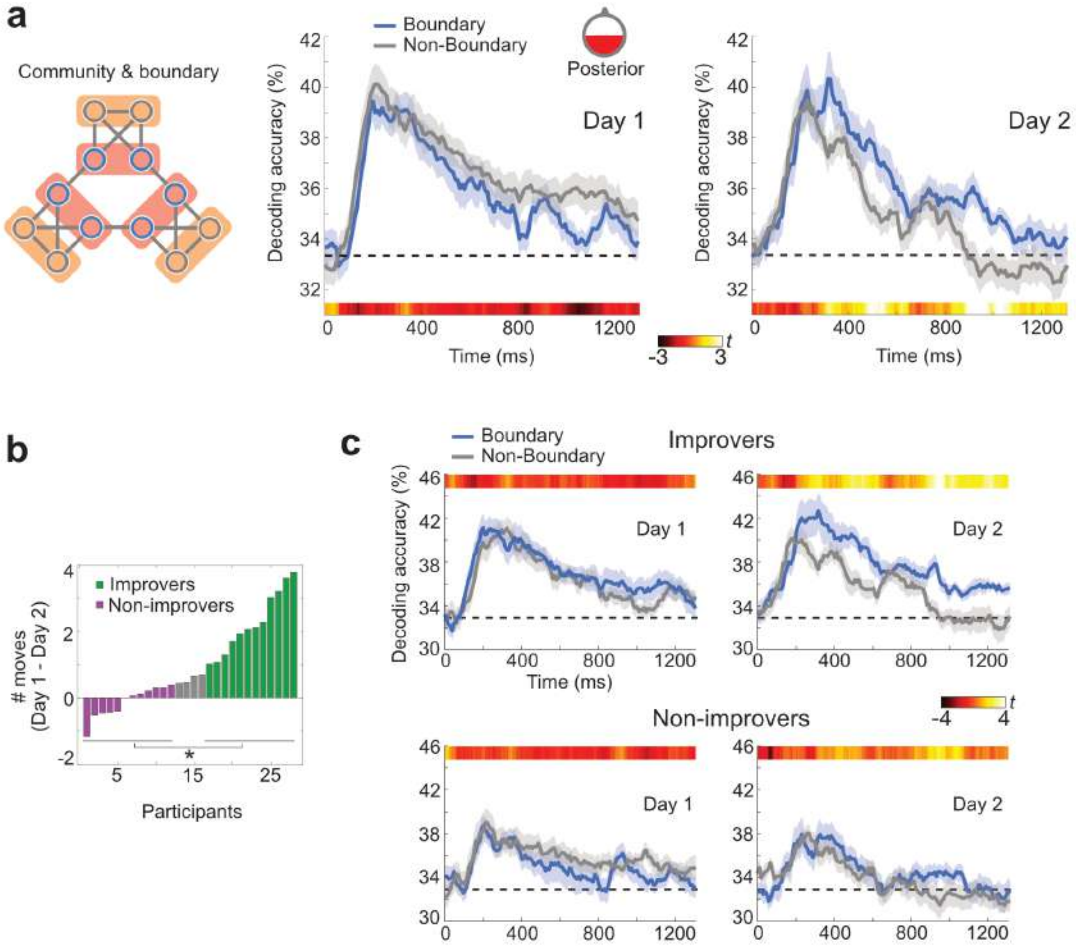


Figure 5.4: Temporal dynamics of decoding accuracy for hierarchical community structure during the task and its impact on behavior. a) Point-to-point average LDA accuracy in discriminating between communities as a function of boundary and non-boundary items for Day 1 and Day 2 considering only posterior scalp EEG electrodes. The results of this analysis showed that boundary and non-boundary-based classifier accuracy was similar on Day 1 but differed on Day 2, being higher ($p < 0.05$, uncorrected) for boundaries than non-boundaries at 300-500 ms and at 900-1100 ms (being the effect in this time window significant after correcting for multiple comparisons, $p < 0.05$ – corrected) from stimulus onset. b) The participants' samples were arranged in an individual bar display, ordered based on the magnitude of their decrease in moves on Day 2 relative to Day 1. c) Point-to-point average LDA accuracy in discriminating between communities as a function of boundary and non-boundary items for Day 1 and Day 2 considering only posterior scalp EEG electrodes for 'improvers' and 'non-improvers' subgroup. In (a) and (c), the thick line represents the averaged accuracy across participants, while the shaded area indicates the standard error of the mean (SEM) across participants. In (b), * indicates $p < 0.05$.

the simultaneous tracking of community structure alongside boundary and non-boundary representations. Furthermore, our findings revealed that participants who showed improvement on Day 2 demonstrated better integration of the hierarchical network structure. This was reflected in the accuracy of the classifier in discriminating between communities based on whether they were better represented by boundary or non-boundary items. These results are indicative that the way individuals perceive and represent a transition structure is heavily influenced by its higher-order organization and how/where different units are connected.

Cognitive and neuroimaging research have shown that the modular organization of a network influences both human behaviour and neural processes. Notably, most of this research has emphasized the individuals' remarkable ability to discern the boundaries separating communities within a network, even implicitly, for example solely by observing sequences of nodes (Karuza, Thompson-Schill, and Bassett 2016; Karuza et al. 2017; Schapiro et al. 2013; Lynn and Bassett 2020; Kahn et al. 2018). Our findings contribute to this literature by showing that this discrimination occurs very rapidly in the brain, upon ~140 ms from item presentation. Moreover, in contrast to previous studies (Schapiro et al. 2013) that primarily focused on the brain response during community transitions in their experimental paradigm, our investigation specifically examined the distinct representations of boundaries versus non-boundaries upon the presentation of items. This approach enabled us to identify the temporal dynamics of memory representations associated with such critical network property and to examine its impact on behaviour. We found that the response pattern associated to boundary and non-boundary representation picked early, < 200 ms from stimulus onset, consistent with previous reports of category-based representation in the brain (Cichy, Pantazis, and Oliva 2014), thereby indicating that the emergence of such important abstract representation of a relational network in the environment appears very early in information processing.

Additionally, we observed a dissociation in the hierarchical relational representations of the task within distinct anterior and posterior scalp EEG regions. This pattern overlaps with a network previously implicated in contextual modulation of behaviour in hierarchical reinforcement learning and cognitive control tasks (Badre, Kayser, and D'Esposito 2010; Choi, Drayna, and Badre 2018; Collins, Cavanagh, and Frank 2014). In previous hierarchical task structure experiments, the emergence of task structure representations, or states, has been shown to enable faster learning, reduced memory load, and greater behavioural flexibility (Frank and Badre 2012; Koechlin and Summerfield 2007). Our findings contribute to this literature by showing that these patterns of representational states can potentially capture distinct network properties during the processes of learning and decision-making. Specifically, the neural response patterns observed in the anterior scalp region appear to primarily capture the crucial property of boundary item detection, which is a key characteristic of modular networks. On the other hand, the simultaneous tracking of community structure alongside boundary and non-boundary representations showed a stronger association with EEG responses from the posterior scalp regions.

In our experimental study, the relationships between items within the network exhibited a concealed hierarchical structure. Understanding how this structural knowledge is transferred to a novel environment constituted an additional aspect we aimed to evaluate in our present design. While a definitive answer to this question warrants further investigation in future research, our current findings provide preliminary support for the hypothesis that generalization could be facilitated through the transfer of relevant representational properties within the network. Empirically validating this notion would involve, for example, quantifying the extent to which the representations of boundary and community states acquired on Day 1 are activated in the novel task on Day 2, where the structural knowledge within the task remains intact while the sensory stimuli is changed.

Inspired by graph theory, we suggest that the brain representation of community and boundaries appears at very early stages of information processing at $\sim$140 ms from stimulus onset. The current findings contribute to the idea that segmentation processes are the backbone of human learning and that the detection of item boundaries in a network influences goal-directed behaviour.

Chapter 6

General Discussion

6.1 Summary of the study results

The primary aim of this doctoral thesis was to provide evidence supporting the hypothesis that event boundaries are temporal moments during which the brain undergoes the process of transforming external inputs into an internal representation of our experiences.

Our results provide evidence that the storage of an event is mediated by a replay-like mechanism which occurs at event boundaries, providing neurophysiological underpinnings for how memory systems might segment a continuous long stream of experience into episodic events. Moreover, we found an increase in ripple activity at hippocampal event boundaries providing evidence for a potential impact of this type of high frequency activity in the segmentation of continuous experiences. And finally, we have found evidence that event boundaries not only play a role in segmenting continuous stimuli but are also instrumental in organizing state-space knowledge into a high-dimensional structure when individuals engage in goal-directed behavior. The results of the three studies helped advance the understanding of how memories are formed amidst continuous stimuli fluctuations, the mechanisms through which it might accomplish so and how segmentation might influence the way we built mental representations of our experiences by shaping the evaluation of options and potential outcomes.

In the following subsections, the main results of each study will be briefly outlined and discussed, along the objectives of the thesis detailed in section 2.

6.1.1 Study 1: Rapid memory reactivation at movie event boundaries promotes episodic encoding.

The main aim of the first study was to assess if just-experienced episodic information is replayed at event boundaries in a context of a naturalistic task. Leveraged by the high temporal resolution provided by EEG data, we found such evidence by observing that a rapid reactivation at event boundaries facilitated the formation of event memories during movie viewing. Memory reactivation was accompanied by a specific left-lateralized anterior negativity ERP effect, which occurred locked to the event boundaries, and may reflect the brain response activity triggered by the detection of a switch in context between the current event and the one that was just encoded. The event-specific patterns of neural activity during encoding were reinstated during later recall, supporting the notion that the process of event segmentation shapes the formation of memories from a continuous stream of stimuli into a structured memory representation that can be accessed at the long term.

To comprehend the formation and organization of memories in real-world scenarios, it is crucial to understand the neural mechanisms that occur in real-time while we encode continuous, lifelike stimuli. Exploring how memories are shaped during audiovisual narratives, such as extended movie clips, offers a promising avenue to test predictions derived from previous studies in more authentic settings. In this study, we investigated whether memory reinstatement, a crucial neural mechanism for memory formation and consolidation, occurred within these ecologically valid experimental conditions. Our findings demonstrate that memory reinstatement indeed takes place, providing valuable insights into how the brain transforms our unfolding experiences into long-term memories that are applicable to real-life situations.

6.1.2 Study 2: Cortico-hippocampal ripple-based coordination during naturalistic encoding.

The goal of the second study was to explore the role of ripples in the encoding of events and its impact in event segmentation in a naturalistic experience. To investigate the properties and interactions of ripples across different brain regions, we employed a similar experimental design as in the above study while utilizing intracranial depth electrodes that were surgically implanted in patients undergoing treatment for pharmacologically intractable epilepsy. This approach allowed us to record and analyze the neural activity within specific brain regions. The results of the study revealed a cortico-hippocampal ripple-mediated interaction that occurred throughout the encoding of an event. The co-rippling interaction between the hippocampus and temporal cortex was correlated with later memory recollection of that event, suggesting that ripples may play a role in facilitating the integration of different event elements across cortical areas. Furthermore, we observed an increase of ripple activity at the hippocampus around event boundaries and within events at the cortical level. This suggests that ripples may be involved in distinct patterns of information processing, which can take place during different temporal periods, with its recruitment at hippocampal event boundaries potentially contributing to the segmentation of events. These findings deepen our understanding of the neural mechanisms involved in memory encoding and emphasize the importance of ripples in the process of event segmentation.

6.1.3 Study 3: Rapid brain signaling of hierarchical relational knowledge in goal directed behavior.

In the third study we sought to assess if boundaries help organize experiences into a hierarchical map representation and aid in goal-directed behavior. In our study participants had to navigate within a hidden relational structure formed by clusters or 'communities' of mutually predicting stimuli, thereby eliciting the emergence of hierarchical event memory representations for picture images, those that linked within and those that linked between *(i.e.*, boundaries) communities. We observed an integration of the community structure by participants, as evidenced by their ability to recognize and distinguish between distinct item types (boundaries and non-boundaries) within the hierarchical representation. Participants successfully acquired specific neuronal pattern representations of both boundary and non-boundary items during the task and these representations were distributed across the entire brain, as evidenced using a LDA classification algorithm. In contrast, the neural response pattern of community structure was predominantly observed in the posterior scalp region rather than anterior. The differential findings between anterior and posterior brain regions may be indicative of distinct neural processes and functional specialization within these regions. By separating participants according to if they show improvement between the two days, we found that, on day 2, the 'improvers' showed greater accuracy in discriminating between network communities when using EEG activity elicited by boundary items than when using non-boundary items. This suggests that boundary items not only contribute to a better representation of the community structure but also enable more effective goal-directed performance.

These findings provide evidence that event boundaries play a crucial role in organizing state-space knowledge into a high-dimensional structure when individuals engage in goal-directed behavior. Moreover, they suggest that event boundaries act as cognitive anchors, enabling effective navigation and manipulation of information within a specific context. By serving as cognitive anchors, event boundaries facilitate adaptive decision-making processes, allowing individuals to make informed choices based on their understanding of the context and the available information.

6.2 What is the specific contribution of memory reactivation at event boundaries?

Research for the past years has shown that the brain can automatically segment the ongoing flow of information into meaningful chunks or events (Zacks et al. 2007). Event segmentation allows us to create coherent narratives and mental representations of our experiences, facilitating the formation of episodic memories that are easier to recall and integrate into our existing knowledge structures. One possible mechanism that may underlie this integration is termed 'replay,' and was originally seen in rodents and shown to occur in moments that could parallel an event boundary, such as when rodents complete a trial (Foster and Wilson 2006).

The discovery that memory-related areas like the hippocampus show increased activity at event boundaries (Ben-Yakov, Eshel, and Dudai 2013; Ben-Yakov and Henson 2018; Baldassano et al. 2017) has led to the proposal that these moments could serve as potential retrieval cues, aiding in memory retrieval and enhancing the overall organization of our memory systems. Indeed, previous research have suggested that event boundaries could trigger a neural reinstatement of the just encoded event (Sols et al. 2017). In Study 1 we extended these findings into a more naturalistic environment where participants were required to encode a 50 min movie. We showed that memory encoding of a particular event was mediated by its rapid reactivation at event boundaries as only events that were later recalled displayed this pattern of reactivation. Reactivating memories at event boundaries may serve as a mechanism to enhance the organization of temporal event memories by strengthening or chunking the recently encoded event. Additionally, it may facilitate the binding of information across episodes by simultaneously activating past and present events.

However, in our study, it is challenging to disentangle the specific contribution of memory reactivation at event boundaries in promoting the encoding of distinct events into memory, the integration of multiple events into a temporally structured memory framework, or both. It is conceivable that during the unfolding of an experience, reactivation may play a role in inferring connections between present and past events, while continually binding together interconnected event models as the narrative unfolds gradually (Griffiths and Fuentemilla 2020). Recent attempts to disambiguate this question have been conducted. For example, in a study by Hahamy, Dubossarsky, and Behrens 2023 they show that reactivation of selected past events is also present at event boundaries reveling a selective mechanism that can piece together relevant parts of an ongoing experience rather than just binding two events that occur concurrently.

6.3 Which neural mechanisms trigger memory reactivation at event boundaries?

Another lingering question from Study 1 pertains to the precise neural mechanisms that trigger memory reactivation at event boundaries and how the process of information binding unfolds during event encoding. One potential candidate is through cortico-hippocampal communication mediated by ripples.

SWR bursts are likely to be an important conduit for interactions between the hippocampus and neocortex. During sleep, neurons in multiple brain areas have been shown to increase their firing activity during hippocampal ripples (Battaglia, Sutherland, and McNaughton 2004) and during wakefulness have also been associated with increases or decreases in cortical activation (Jadhav et al. 2016). Given so, during the encoding of an event, one would expect the communication between these areas to be necessary to ensure the integration of perceptual details with contextual information. Indeed, ripples have been associated to increased activity in hippocampus and the default-mode network (DMN) in both humans and animal models (Higgins et al. 2021; Kaplan et al. 2016; Norman et al. 2021). The same brain regions have been shown to be involved in event segmentation (Reagh and Ranganath 2023; Baldassano et al. 2017) so it is reasonable to think that ripples may play a role in event parceling. DMN regions are known to carry activity patterns over entire scenes of a movie (Bird et al. 2015; Chen et al. 2017), and different subnetworks are responsible for representing contextual and situational information (*i.e.*, posterior-medial network; Ritchey and Cooper 2020) or information about entities, such as objects and people (*i.e.*, anterior temporal network; Bonner and Price 2013). The hippocampus has direct anatomical connections to DMN areas and, out of the resting state networks, makes preferential functional connections with the DMN. Moreover, activity patterns in DMN regions remain stable as an event unfolds, but these patterns shift abruptly at event transitions, where activity in the hippocampus is on the contrary, particularly active and correlates to the correct encoding of an event (Baldassano et al. 2017; Ben-

Yakov and Henson 2018). All these findings together suggest that a dynamic interplay between the DMN and the hippocampus is required during encoding of an event in order to correctly bind different aspects of the perceived experience into one unified memory trace. In Study 2 we have also shown that ripple occurrence takes place differently across the brain regions used in this analysis, with brain regions corresponding to the DMN showing higher ripple activity occurring within event and a decrease around event boundaries whereas the hippocampus showed the opposite pattern. During the encoding of a dynamic event, the recruitment of ripples at different moments and in different areas may serve as a computationally efficient strategy to simplify complex events by focusing on key components. By selectively engaging ripples at specific time points and in specific brain regions, the brain can extract and consolidate essential information from the event, streamlining the encoding process. A peak in hippocampal activity and a shift in cortical patterns at the boundary might temporarily disrupt the drift of temporal context, resulting in event segmentation.

In Study 2 we showed the first evidence for an involvement of ripples in the encoding of naturalistic ongoing activity. During the encoding of an event, ripples were observed to co-occur in both the hippocampus and cortical areas, but in different temporal orders. Specifically, the temporal cortex was found to precede the hippocampus, which in turn preceded the frontal cortex. This intriguing finding provides evidence for the dynamic interplay between cortical regions and the hippocampus during encoding.

6.4 How do the ripples found in our study compare to previous rodent studies?

While the investigation of ripples has predominantly focused on rodent models, there has been a notable surge in research characterizing these phenomena in humans over the past five years, including our own study. Through this research, notable similarities and important distinctions have been uncovered across species. Below, I highlight some of the prominent differences observed:

Ripple Frequency: The frequency range of ripples can vary between rodents and humans. In rodents, ripple oscillations typically occur within the range of 150-250 Hz (Buzsáki 1986), while in humans, they tend to fall within the range of about 80-140 Hz (Axmacher, Elger, and Fell 2008; Vaz et al. 2019; Staresina et al. 2015; Vaz et al. 2020;Norman et al. 2021; Sakon and Kahana 2022; Kunz et al. 2022). This frequency difference may reflect species-specific variations in neural circuitry and physiology as ripple frequency is also known to slow down with brain size (e.g., SWR frequency in monkeys is similar to ripple frequency in human subjects; Skaggs et al. 2007). Most studies assessing for the presence of ripples in humans have used intracortical recordings from patients with epilepsy. Given so, we cannot absolutely exclude the extent to which the ripples identified in these studies, including ours, are reflected by the presence of pathological activity. Nevertheless, many correlations between ripple occurrence and behavioral measures have been shown proving that, at least in part, the ripples found in these studies must reflect physiological changes.

Functional impact: Ripples in rodents have been closely associated with the coordinated reactivation of place cells in the hippocampus, which is believed to play a role in memory consolidation, learning and planning of upcoming actions (Nádasdy et al. 1999; Foster and Wilson 2006; Diba and Buzsáki 2007; Karlsson and Frank 2009; Ego-Stengel and Wilson 2010; Jadhav et al. 2012). In humans, ripples have only been explored in the context of memory tasks and are thought to be involved in memory processing. However, their precise functional correlates are not well understood. Studies in awake humans showed that ripple rates increase when subjects encode new memories (Norman et al. 2021) and when they freely recall memories (Sakon and Kahana 2022), implicating ripples in both memory encoding and retrieval. Human hippocampal ripples have also been shown to coordinate the activity of specialized cellular populations to facilitate links between stimuli (Kunz et al. 2022) and in our study to play a potential role in binding different aspects of perceived experience into one unified memory trace. And so, the current results advance our understanding of human ripples, but this knowledge is still relatively limited and disperse, and more research is needed to uncover their precise characteristics and functions.

Ripple Dynamics: Some of the basic characteristics of ripples seem to be different between rodents and humans. For instance, the duration of ripples in rodents tends to be shorter compared to humans (Axmacher, Elger, and Fell 2008). Some studies also point for a potential effect of ripple duration in memory, with long-duration ripples increasing in situations demanding memory in rats (Fernández-Ruiz et al. 2019). In our study, however, we found no significant difference between ripples that occurred in events that were later remembered to ripples occurring in events later forgotten, so if this effect is transferable or not to human ripples still needs to be explored.

Ripple wide-brain occurrence: Research in rodents suggests that ripples can occur not only within the hippocampus but also in the neocortex, and that ripple coupling between regions can enhance learning (Khodagholy, Gelinas, and Buzsáki 2017; Todorova and Zugaro 2020). In humans, we see that ripples also occur at different cortical areas and can couple within and across brain regions. In Study 2 we find evidence for the co-occurrence of ripples in the hippocampus and cortical areas, with hippocampal ripples either preceding or advancing cortical ripples. This co-occurrence was sometimes correlated to whether an event would later be recalled, pointing to a potential role of ripples in mediating the communication between different brain regions.

Ripple associated replay: In rodents, studies have shown that ripples tend to exhibit a sequential pattern, with specific sequences of ripples recurring during sleep and rest periods (Foster and Wilson 2006; Pfeiffer and Foster 2013; Diba and Buzsáki 2007). These sequences are thought to reflect the replay of previously experienced events or the reactivation of memory traces, contributing to memory consolidation and spatial navigation. In humans, while the precise characteristics of ripple associated replay is still being investigated, some studies suggest that ripples may also exhibit sequential patterns associated with memory processing (Vaz et al. 2020). However, this study focused on sequencing during memory retrieval and so the impact of ripples in neural replay of certain information during memory encoding still needs to be elucidated. One could speculate that the rapid reinstatement observed at boundaries in Study 1 may be directly related to the increase in ripple occurrences around hippocampal boundaries in Study 2. This increase in ripple events could potentially be involved in replaying the sequence of elements encoded during the boundary event. However, we did not find a significant impact of this ripple increase on later recollection of the event, as we observed with the neural reinstatement in Study 1. This does not, however, rule out the possibility of a correlation between ripple occurrence and replay during these moments. It is possible that the ripple-associated replay is present but is instead related to the replay of past events rather than the temporal binding of the two sequential events, which has been specifically linked to the hippocampal neural reinstatement observed at boundaries (Hahamy, Dubossarsky, and Behrens 2023). This may explain why no direct link between the ripple increase at boundaries and later memory recollection of the event was found. It is also worth considering that the neural reinstatement observed may not necessarily be the most appropriate measure to assess what is referred to as neural replay in the context of rodent literature. Further research is needed to determine whether a connection exists between these two boundary phenomena.

Taking it all together, our paradigm and analytical approaches revealed that a neural reactivation occurs at event boundaries and is essential for memory encoding, similarly to the neural replay mechanism found in rodents, thus bridging the neural reactivation/replay findings in the two species. However, the mechanistic way through which this might be accomplished and what it represents is still a matter of debate, as in rodents we usually see an association between neural replay and ripples whereas in our human studies the association between the two was not clear.

6.5 Forming relational map representations and its implications for event segmentation

For a while now that the hippocampus has not been seen as a traditional memory or decision-making focused area but more as an area responsible for the creation and update of internal models of the world. To study how the hippocampus might accomplish this, researchers have made use of concepts normally applied to network science. By constructing modular networks, where states are conceptualized as nodes in a graph with edges or connections representing possible transitions between them, we can study how the brain constructs this map-like brain representations in a unique and ecologically valid framework (Karuza, Thompson-Schill, and Bassett 2016). Research in statistical learning has revealed that modules, which are communities of densely connected nodes within transition networks, can be observed in brain imaging data (Schapiro et al. 2013) and that the hippocampus is particularly involved in learning the structure in these community-based sequences (Schapiro et al. 2016). In Study 3, we applied a similar graph like task design to assess if event boundaries were the driving-force in the organization of a state-space experience into a hierarchical map representation. Contrary to previous research, where participants simply performed a random walk of the map (Schapiro et al. 2016;Garvert, Dolan, and Behrens 2017), in Study 3 participants had to learn the statistical regularities while being instructed to find specific images from the map. Even though they needed to engage in highly adaptative goal-directed behavior, as in our task design the goal changed on every trial, participants were able to learn the structure of the map and improve their performance from early on. We found that participants successfully detected item boundaries within the network, which was associated with fewer moves required to reach a goal. Our results add evidence to the hypothesis that event segmentation might play a crucial role in goal-directed behavior. Overall, we hypothesize that, by identifying event boundaries, individuals can differentiate between different phases or stages of a task which would allow for the integration of relevant information and the planning of actions based on the current event's goals.

The fact that participants which showed improvement between the two-day sessions also exhibited greater accuracy in discriminating between network communities from EEG activity, when relying on boundary items, could be indicative of some sort of transfer of knowledge from Day 1 to Day 2. While a definitive answer to this question warrants further investigation, our findings provide preliminary support for the hypothesis that in constructing mental representations of our experiences one can generalize and adapt to novel environments. Event boundaries may provide the natural breakpoints for this evaluation and generalization process. As individuals approach an event boundary, their cognitive systems generate expectations about what might occur next (Kurby and Zacks 2011). The replay-like mechanism at event boundaries identified in Study 1 could provide the neural mechanism through which the brain can form such predictions. How this boundary replay directly impacts the creation of the mental map representation and how it impacts goal-directed behavior requires however future investigation.

Nevertheless, in this thesis our results provide evidence that suggests that event segmentation plays a crucial role in facilitating the interaction between episodic memory and decision making.

6.6 Limitations and future directions

6.6.1 Link between ripples and replay in humans

Our findings from Study 2 propose that a cortico-hippocampal ripple-based communication during encoding plays a pivotal role in the encoding of events. In this study we analyzed data from temporal and frontal cortex. However, other brain regions are also involved in event encoding and it would be of value to conduct a more extensive search of weather and how ripples may impact memory encoding in other areas, such as other DMN and MTL regions. Nevertheless, some limitations related to the nature of this type of recording reduced our sample size. Indeed, the recruitment of iEEG data from epileptic patients comes with challenges. For example, during the time of my PhD thesis, data from almost 20 patients has been acquired. Due to the variability in the number and placement of electrodes across subjects, which was determined solely by clinical requirements, we were, however, limited to analyzing data from only 10 patients who had hippocampal electrodes implanted. It is important to acknowledge that data acquisition was also significantly restricted during the recent COVID-19 pandemic, resulting in limited access to hospitals and subsequently reducing the number of available patients for analysis. Therefore, not only was the sample size reduced, but also the range of regions that could be examined. Moving forward, it is crucial to continue gathering this dataset to further extend the findings.

As already mentioned in the above paragraphs, a better understanding of the potential differences in ripple functions between rodents and humans also needs to be established. Particularly, if the co-rippling activity found in Study 2 is in any way related to neural replay as we know it occurs in rodents (Foster and Wilson 2006; Pfeiffer and Foster 2013; Diba and Buzsáki 2007). Ripples have been shown to exhibit sequential patterns associated with memory processing (Vaz et al. 2020) during memory retrieval. We can hypothesize that sequential replay should also occur during memory encoding as we know that memory is reactivated at event boundaries in the hippocampus, both for past events (Hahamy, Dubossarsky, and Behrens 2023) and the just encoded one (Study 1). The hippocampus is known for its ability to not only recombine elements of an original trace but adding or subtracting individual contextual features resulting in a new memory trace, and so neural replay as a form of sequencing during ripple occurance could be a possible mechanism through which this could be accomplished, where information from past events is integrated with new event information at event boundaries. In Study 2, we did not find a significant impact of this ripple increase on later recollection of an event and could not look for pattern sequentiality. One potential way to overcome this limitation could be through the acquisition of single-unit recordings. Single-unit recordings offer a unique and invaluable window into the inner workings of individual neurons, which could provide detailed insights into the firing patterns and temporal dynamics of cell firings during ripples at event boundaries and point to any sequentiality.

An alternative possibility is that sequencing during event encoding may be facilitated by different mechanisms, so that ripple mediated sequencing is not the one related to the neural reinstatement we see at boundaries and instead it is due to a phenomenon called theta sequencing. During maze navigation in rats, specific combinations of hippocampal pyramidal cells become active in successive cycles of theta oscillations. At the trough of the theta cycle, the group of cells that are most active corresponds to the rat's current location. Adjacent to this group, other neurons fire spikes during the descending and ascending phases of theta, representing past and future locations, respectively. This discovery was initially demonstrated by O'Keefe and Recce 1993 and further supported byDragoi and Buzsáki 2006. In their experiments, they observed a systematic shift in the timing of spikes from a place cell relative to the phase of the ongoing theta oscillation. They termed this phenomenon phase precession, which revealed a unique and consistent relationship between spike timing and theta phase. This demonstration of phase precession provided the initial experimental evidence for a long-presumed temporal "code" within the hippocampus. Since then, the phase oscillation of theta activity has been shown to influence successful memory encoding and retrieval (Hasselmo 2005; Clouter, Shapiro, and Hanslmayr 2017) and to have some important distinctive features to the ones found in rats (Jacobs 2014). Gamma oscillations are frequently seen to nest within an ongoing theta cycle (Colgin 2015), a phenomenon described as theta-gamma phase coupling. These phenomenon has also been correlated to successful memory formation in several studies (Heusser et al. 2016; Tort et al. 2009). The theta rhythm can transiently increase synaptic plasticity (Buzsáki 2005), and can serve to organize the order of individual elements within an event (Colgin 2015; Jensen and Lisman 2005) and so it is as likely positioned to be responsible for the biding of information within event as ripples are. Using the same dataset as in Study 2 could allow for the testing of the event conjunction framework, a model proposed by Griffiths and Fuentemilla 2020, which proposes that theta-gamma coupling within the hippocampus could be used to maintain the temporal sequence of the elements of an event and at an event boundary replace the previous event 'model' by a new one. Exploring this hypothesis would help uncover a novel and fundamental component of how memories are segmented in daily life.

6.6.2 Neural replay during goal-directed behavior

The findings from Study 3 suggest that event boundaries play a crucial role in organizing state-space knowledge into a high-dimensional structure when individuals engage in goal-directed behavior. Replay has been suggested as the mechanism that allows animals to integrate current and past experiences in order to successfully learn and plan upcoming behavior. Replay sequences were observed at points where animals were required to make decisions (Johnson and Redish 2007) with trajectory replay predicting future arm choices during spatial navigation (Xu et al. 2019). By replaying neural activity patterns associated with different choices or actions, the brain can simulate potential scenarios and evaluate their potential outcomes. This replay-based evaluation assists in the selection of optimal strategies or actions in future goal-directed behavior. In Study 1 we find evidence that the binding of information into long-term memory at boundaries could also happen through the triggering of a rapid replay like mechanism, and so it is reasonable to assume that these moments may be important to determine which actions to take in the future in a process mediated by this replay like mechanism.

In the context of Study 3 one possibility would have been to assess if the transition between clusters (*i.e.*, at event boundary transitions) was marked by a reinstatement of the previous selected item, through the use of representational similarity analysis, which would have helped us find a link between this boundary replay like mechanism and goal-directed behavior. However, the way our study was currently designed did not allow us to look for reinstatement at the transition points between clusters. This is because our analysis was performed using the signal corresponding to the moments when participants were cued individually with the items from which they would later have to make the selection from. The moments where the final decision to select an item was being made would have been the ideal period to assess for this reinstatement, as we hypothesize this would be when participants had to assess the connections between items and its outcomes. However, as the signal from these moments contained information from other items on screen and is affected by the movement artifacts resulting from the act of pressing a button to select their choice, we could not perform the suggested analysis. In the future it would be interesting to adapt this task in a way that could allow us to look for reinstatement of certain items at the choice moment. Perhaps by adding a localizer at the beginning of the task, where participants are simply presented with the items later seen during the main task, one could later track pattern reinstatement for specific items during each trial. This could be possible by using the signal acquired during the localizer to train a classification model to look for those specific patterns during the task. A similar approach has been conducted in a fMRI study by Crivelli-Decker et al. 2023 to show that during planning, the hippocampus carried context-specific information about individual sequences to a goal. Their results suggest that goals and other salient locations exert a powerful force on spatial and non-spatial maps in the brain and so, paralleling that to the results of our task, we could hypothesize that boundary items represent such moments.

Here, and because of the nature of the EEG recordings, we were also not able to pin-point which brain areas were responsible for our findings. Our results only suggest that boundary and non-boundary representations were distributed across the entire brain whereas the community structure representation was predominantly observed in posterior scalp regions. Making use of techniques with better spatial resolution could be a potential way to disentangle this relation. Using intracranial EEG recordings could bring not only the advantage of assessing the role of hippocampus in this process but also the possibility to assess if there is any neural signature associated with a replay-like mechanism present at boundaries, such as ripples which are known to be associated with replay at decision points (Johnson and Redish 2007; Jadhav et al. 2012).

Another potential follow-up to this project would be through the application of Reinforcement Learning (RL). A recent body of work as applied RL algorithms to assess how memory is used to guide decisions in a similar set of tasks as the one applied in this study (Garvert, Dolan, and Behrens 2017; Stachenfeld, Botvinick, and Gershman 2017; Momennejad 2020). The model is used to learn the structure of a state-space map which can then be used to compare with participants behavior. By applying different types of models, and varying their defining variables, one can assess the contribution of different brain function principals to participants behavior. One particular set of algorithms, the successor representation, has been proving quite fruitful in allowing us to understand how representational learning, replay and prospective planning help acquire multi-scale predictive maps given that it's eigenvectors mimic grid field representations (Stachenfeld, Botvinick, and Gershman 2017). In the future, researchers could leverage these RL algorithms to investigate the role of replay and prospective planning at transition points within a task similar to the one used in Study 3. This investigation could shed light on how memory, replay, and the identification of event boundaries influence goal-directed behavior and the creation of mental map representations.

6.6.3 Neural replay and ripples during memory recall

The studies included in this doctoral thesis focused in investigating how memory formation occurs during encoding. In Study 1 we showed that event-specific patterns of neural activity elicited during encoding were reinstated at later recall and in Study 2 we investigate the cortical-hippocampal ripple interaction during encoding.

How do humans retrieve the elements that constitute the event? How does this differ from retrieving single lab-based material used commonly in the memory research in the past decades such as words and images? The experimental design included in this thesis is not ideal to answer to this question. In a free recall task, such as the one employed in the current studies, participants not only exhibit variations in the time taken to describe the encoded stimuli, but also provide different levels of detail and varying accounts. These individual differences make it challenging to precisely identify the specific moments when one event concludes, and another begins. In Study 1 a data-driven segmentation method was applied to obtain the most probable division of a given signal for a given number of events. However, this algorithm requires a certain number of features to be inputted. In Study 1 this corresponded to the different EEG electrodes, but in Study 2 the reduced number of available electrodes made it impossible to apply the same model and so we could not explore how the cortico-hippocampal ripple-based interaction impacts and occurs during later memory recollection. To expand our results into recall one would perhaps need to acquire new data where participants perform a cued recall instead of the free recall applied here. This would allow one to recover and study brain activity at event boundaries and during within event retrieval and assess if ripples are a marker of retrieval in humans, as observed in rodent studies, as well as if they are needed for successful retrieval. By unraveling these interconnected dynamics, we can gain valuable insights into the intricate mechanisms of memory formation and retrieval.

Chapter 7

Conclusions

- **The brain possesses the ability to perceive and retain information by breaking down the continuous flow of experiences into distinct events. This remarkable cognitive process allows us to make sense of the world around us, creating a framework for understanding and recalling our memories. Each event represents a meaningful unit, often encompassing a specific time, place, and context. These episodic events act as building blocks for memory formation and retrieval, allowing us to recall and reflect upon past experiences with precision.**

- **A rapid neural reinstatement occurs at the end of each event and impacts if an event is later recalled or not. This evidence provides the first proof for an electrophysiological signature related to how event segmentation shapes memory formation. By showing that this neural mechanism, critical for episodic memory formation and consolidation, also takes place under ecologically valid experimental circumstances our findings offer insights into how the brain shapes the unfolding experience into long-term memory that can be generalized to real-life.**

- **A cortico-hippocampal ripple-mediated interaction occurs throughout the encoding of an event. This interaction plays a significant role in integrating diverse elements across cortical regions during encoding and is crucial for correct memory formation. These findings highlight the intricate mechanisms underlying memory encoding and provide insights into the role of ripples in event segmentation and memory consolidation.**

- **Ripple activity increases at hippocampal event boundaries and within events at the cortical level, with demonstrates the existence of distinctive patterns of information processing during different temporal periods. This emphasizes the importance of ripples in the process of event segmentation and suggest that hippocampal ripples could potentially be used as event boundary markers.**

- **During the navigation of intricate abstract environments, participants have the ability to identify and differentiate between different types of items, namely boundaries and non-boundaries. In this process, the brain rapidly generates distinct neural patterns associated with event boundaries. These patterns play a vital role in organizing** knowledge about the state-space and contribute to the creation of a comprehensive representation of the environment. As a result, this enhanced representation enables participants to perform tasks more effectively and with greater focus on achieving specific goals.

- Event boundaries serve as cognitive anchors, providing natural breakpoints for evaluation and manipulation of information within a specific context, thus facilitating informed choices based on contextual understanding and available information. The segmentation process provides the opportunity to consider the contextual factors and available information specific to each event, enabling us to make more informed decisions.

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