How do we recall childhood memories?

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Reconstructing childhood playground memories

If you ask a neuroscientist "how do we remember our lives?", she'd say it is a long and fascinating discussion. She'd tell you that to recall a remote memory you need to use your prefrontal cortex, which is where old memories are drawn, and you need the **hippocampus** – a sophisticated brain structure without which we cannot make new memories and cannot recall details.

Hippocampus is truly remarkable, she'd say, because it can fuse various sensorial details from a memory into a cohesive plot of an episode you have lived. And this enables us to keep an autobiographic story of who we are. The hippocampus is remarkable because it contains concept neurons, place neurons and grid cells that code your location in space and enable the making of mental maps of not only physical but also relational space. To perform such complex functions, it carries out pattern separation and pattern completion. And in order to do that, the neurons in one of its sub-structures, CA3 (cornu ammonis 3) work together in what can be computationally modeled as a complex algorithm called autorecursive or fully **auto-associative network**.

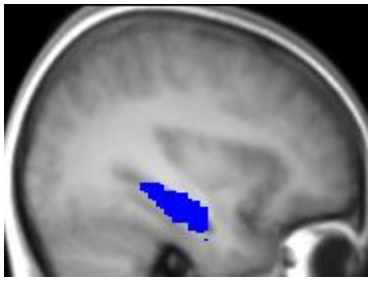
Although recollection can be evoked by various cues (such as smell, music or an emotion), an important component of every episodic memory is one's **physical location** when the memory is formed. In the hippocampus there is a network of neurons called **place cells**. Each place cell typically activates in correspondence with a specific region of one's physical environment. Collectively, the regions of activation of all hippocampal place cells cover one's entire environment, and the level of activity across all the cells in combination provides a precise signal encoding one's present location. Operating upstream of the hippocampus is a region called the medial entorhinal cortex, which contains neurons known as **grid cells**. Each grid cell activates in correspondence to multiple locations that are arranged as a triangular grid [1].

How does location help us to remember?

In one study, when young adults were asked to recall an episode from the past year of their lives, many reported spatial context as a preferable point of access into their memories, and differences in the tendency to benefit from spatial memory cues was related to the size (volume) of their hippocampal area cornu ammonis 1 (CA1) [2].

Childhood memories are special in that they are formed in a brain that is not yet physically developed but also does not have pre-existent **schemas** within which the experience could be embedded and so the level of memorized detail is typically very high. In contrast, autobiographic memory in older adults is more semantic in nature (with less contextual detail).

In the following, I will explain in more detail what happens in the brain when we recall a memory.



Hippocampus

Recollection

Episodic memories are a type of explicit (or declarative) memory that denotes the recall of, for example, what we had for breakfast yesterday and what we did at school in childhood. Episodic memory thus refers to recollection of personally experienced events and their contextual details (i.e., what, where, when); the capacity for mental time travel of past and future events; and a sense of autonoetic consciousness [3]. Thanks to episodic memory, we are able to "re-experience" an event in the past and project ourselves into an imagined event in the future.

In order to recall an episodic memory, we use areas of the brain located in the medial temporal lobes. Within this area, the main structure is the hippocampus – a seahorse-shaped ridge of gray matter tissue that takes up between 3 to 3.5cm^3 in adult humans (compared to 320 to 420 cm^3 for the volume of the neocortex) [4].

But where are these memories stored? Neuroscientific evidence shows that memory is held in specific populations of neurons, referred to as **memory engram cells**, and their associated circuits [5]. The term engram refers to a specific pattern of activity across a neuronal population that is activated during memory encoding and retrieval.

The sight of a familiar person or the sound of this person's voice, for example, triggers a cascade of brain processes that creates a representation leading to the recognition of the person and the recollection of details related to him or her. How is this possible?

The holistic retrieval of complex event memories is thought to be the hallmark of episodic memory, underpinning the **'recollective' experience**. Episodic recollection is distinct from other forms of memory retrieval, such as retrieval of semantic associations (for example, associating Marilyn Monroe with New York City) or feelings of familiarity. In such a memory, all sensorial (sounds, colors) and affective (how did that make me feel) aspects of an event are retrieved, painting an entire scene, rich with contextual elements, even with those that might be incidental to the content of the event. In the brain, episodic recollection from a single cue indeed leads to reactivation of various linked elements that are coded in different cortical (sensorial) areas of the brain [6]. Evidence from human neuroscientific research shows that episodic memory is the key function of the **hippocampus**, which is **binding together the elements of an event**, allowing for their retrieval via a process called **hippocampal pattern completion**, and subsequent reinstatement in the neocortex.

We know that the hippocampus serves to patch the memories from fragments and bring back the entire experience. Some neurons in the hippocampus and surrounding areas have been discovered to be **"concept cells"**: single-neuron recordings in humans have identified cells that are reactivated only during the free memory recall of a particular concept (a person, landmark or episode) (Gelbard-Sagiv et al., 2008). They respond to the subjective meaning of a particular concept, including the

voice of the person, their name spelled out in letters, diverse pictures of them, as well as of people closely related to them [7]. Thanks to these neurons, the hippocampus is able to re-create an experience from a single bit of information, such as the thought “playground”.

The process in the medial temporal lobe that serves to re-create such a re-experience is called **pattern completion**. It is the retrieval of all constituent elements of an event (for instance, an entire episode from one’s childhood) when presented with a single element as a cue (for instance, the square where a playground used to be located). An event memory might bind together the location we were in, the person we met and the toy they gave us.

Remarkably, the brain is able to **reconstruct** the entire holistic memory from just one element or cue.

Researchers have demonstrated how this process envelops in healthy human volunteers using an indirect noninvasive method of imaging neurons, functional magnetic resonance imaging (fMRI) [6]. In an associative memory task, they found that the hippocampus binds the multiple elements of an event into a single coherent memory trace during the first time these elements are seen, during the first stage of memory formation called **encoding**. This enabled pattern completion when the participants were later asked to retrieve the associated memory from one cue.

The bilateral anterior hippocampus was more strongly activated during the encoding of a last element of an episode, indicating that it was performing the binding (or gluing) of various elements of a memory into one cohesive memory. This fMRI activation was a signature that when the last single element was presented, the hippocampus was recovering all previously memorized elements to complete the memory pattern. At the same time, the retrieved elements of the recalled episode were **reinstated**, that is they were reactivated in the same cortical structures that served to encode them (for instance, the memory element “a person” activated the medial prefrontal cortex; a place activated the parahippocampal gyrus). Importantly, the activity in those cortical areas correlated with that of the hippocampus, which confirms the role of hippocampus in binding related elements to recollect an entire memory when only one cue is provided.

This experiment also demonstrated one other interesting side-effect of this reconstructive process of memory recollection. Sometimes the participants recalled all related elements, whether relevant to the task or not. They therefore accidentally recalled **false memories**. Because the cue leads to incidental reinstatement of all related elements, also those that did not co-occur in space and time, when the hippocampus brings them back during recollection, they may eventually end up being bound to the original episodic memory. This is the case when a recollected memory is once again made “fresh” and therefore labile – but certain conditions must first be present. It is certainly the case with new memories, those that have not undergone the several stages of consolidation, however, in general, any recollected memory may either become consolidated more strongly for better, longer lasting memory, or it may become updated or bound with some novel elements. This is because the life of a memory is a dynamic process rather than static storage (cf. Summary: the making of a memory).

False memories

Since episodic memory is reconstructive, it is possible to imagine that sometimes **the reconstruction is imperfect**. Some details may be missing due to forgetting and some new ones may **fill in** their place to form what will appear to be a holistic episode. Interestingly, the nature of the process of recollection may incidentally form false memories.

As hinted earlier, the act of recalling a memory renders it labile and in some cases, highly susceptible to modification [8]. In humans, memory distortions and illusions occur frequently, which often results from incorporation of misinformation into memory from external sources[9]. The recall of both false and genuine memories has been reported to result in robust hippocampal activity in humans but specific brain regions responsible for the generation of **false** memories have not yet been delineated[5].

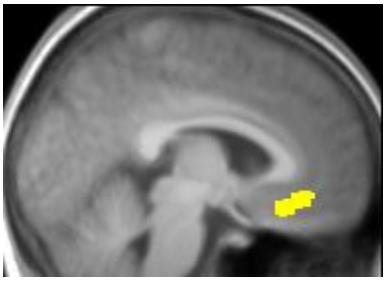
Episodic recollection is not generally veridical, and people often falsely 'recollect' some elements of an episode with high confidence. One mechanism via which such false elements may be brought to mind and implanted in an episode is through the above-mentioned pattern completion. Due to the presence of a single coherent event engram, all types of elements are reactivated causing a subjective sense of confidence in remembering the different aspects of the same event to be related [6]. This is because the same binding mechanism that enables us to associate many elements of an episode and bring it back in recall, also binds in other elements, even if they had not taken place simultaneously.

In one study, human participants toured a museum while wearing a camera that recorded the event [10]. At a memory test that followed, they were presented with photos taken during their tour, along with photos taken from a different tour of the same museum. Their recognition memory was better for those photos that matched highly reactivated memories, but importantly, reactivation also increased false memories of the novel photos. At the same time, false recognition of the novel photos was associated with activation of the anterior hippocampus and the **ventro-medial prefrontal cortex (vmPFC)**, regions implicated in **memory transformation** and described in more detail below[11].

Another mechanism by which false episodic memories can be implanted is when the memory of a past experience becomes associated with a current external event of high valence. Valence refers to emotional importance, such as fear or anticipation of a meaningful reward. And considering the fact that humans have a rich repertoire of mental representations generated internally by processes such as conscious or unconscious recall, dreaming, and imagination, this path to formation of false memories is probably one frequently taken by many human brains every day. In fact, implanting false memories using this mechanism has already been performed using direct optogenetic neural stimulation of fear engram cells (negative valence) in the medial temporal lobe areas in mice [5]. Such studies also additionally confirmed that a reactivated memory is open to integrate novel information that is presented at the same time.

However, important borderline conditions must be present for an old memory to first render it labile and then to incorporate new information – a next process in the life of a memory, referred to as **reconsolidation**. Luckily, many old memories, especially those well-rehearsed ones, are more stable and resistant to updating upon recollection [12].

Therefore, the formation of false memories in humans often occurs as a result of recombining mnemonic elements of discrete experiences into a new, reconstructed memory that is not a true representation of the past. Importantly, such "implanted" memories are not formed from scratch but rather require pre-existing memories as a scaffold onto which new experiences can be incorporated to update the memory itself[5].



Ventro-medial Prefrontal Cortex

Transformation of memories over time

Research has shown that over time, the activation of hippocampus during recall decreases as the memory engram is distributed across the cortex (and especially in the vmPFC) and generalized, semanticised and eventually embedded in a **schema**.

This process of extracting gist from an episode and linking it to extant schematic older memories begins already at encoding, where the life of a memory begins. Unless you are a neonate, no memories are created in a vacuum. Every new memory is linked to what you have experienced before to keep your life story cohesive and continuous [13,14]. Therefore, the stable, previously rehearsed (or similar) elements of a memory, are readily picked up and retrieved as you experience something new. This is how we are able to make associations even when learning a completely foreign-sounding new language (because we already have the schema of what a "language" is) [15]. The simultaneous formation of schemas makes learning easier with experience as the schemas accumulate. Therefore, a life rich in experiences is a life rich in schemas and that is why it is perhaps more difficult to surprise us the older we get…

It has also been speculated that it is due to the mechanism of schematization that begins at encoding that leads a person to accept a false memory as own or that as a result of having a strong memory schema, the confidence in an fake detail is increased leading to a false sense of accuracy [16].

Transformation of a memory of an episode is visible already over the course of 7 days.

The activation of hippocampus declines as vivid perceptual and contextual details fade due to forgetting but retrieval of the 7-day old memory is also supported by strong activity in the ventromedial prefrontal cortex (vmPFC), consistent with the idea that the memory becomes distributed and supported by a cortical network over time but continues to depend on the hippocampus for retrieval. In fact, the strength of activation of the hippocampus correlates with the accuracy of recall for episodic details even weeks and months after viewing a movie clip [17]. Another study showed that tracking the retrieval of implanted event memories two weeks to two years after the encoding, they could be better decoded from activity within the vmPFC rather than the hippocampus [18].

The intriguing shift in hippocampal informational maps may suggest that rather than 're-activating' the same hippocampal-neocortical ensembles that were active during encoding, the vmPFC (and/or other cortical regions) provide the hippocampus with informational units which it uses to construct a coherent representation 'on the fly' rather than re-construct a previously activated pattern (McCormick et al., 2017a).

Autobiographic memory

To recall events from personal history that integrate self-related knowledge with experienced events, we use autobiographic memory. This type of memory is shaped by many factors, including self-schema, goals, emotion, culture, age, gender, and genetics. The vastness and diversity of past personal experiences captured in our autobiographic memory define who we are, help us relate to other people, and enable future planning [16].

Indeed, thinking about the past and imagining the future are two sides of the same coin in the brain, sometimes referred to as *mental time travel*. Indeed, fMRI patterns of activation during autobiographic memory recall and future imagination are similar [19]. Moreover, research on patients with autobiographic amnesia shows that the hippocampus is necessary not only to remember but also to generate details in imagining the future [20].

Understanding entire decades-long life of a human memory remains elusive due to technical difficulties in carrying out such neuroscientific research in living humans. As a result, we do not precisely know the circuit or cellular mechanisms for this process nor its molecular characteristics [15]. Most likely, the life of a memory continues according to what is known as the multiple trace theory: 1) an initially formed memory remains dependent on the hippocampus for as long as it is available; 2) a hippocampal memory over time supports the development of a schematic version of the memory in the neocortex (retaining the gist of the original memory, but fewer contextual details); 3) a dynamic interplay exists between the cortical and the hippocampal versions of the memory such that one or the other may be dominant depending on the circumstances at retrieval [15].

Specifically, the multiple trace theory states that each time an episodic memory is retrieved it is subsequently re-encoded, thereby leading to the formation of multiple traces within ensembles of hippocampal–neocortical neurons and therefore long-term storage of information occurs in a distributed cortical network where different modality-specific 'fragments of a memory' co-exist across different sensory cortices [15].

Forgetting and childhood amnesia

From behavioral studies we know that perceptual and contextual details decline more rapidly than central schematic elements, which is consistent with the transformation of memory described in the previous section. But why does this occur?

Up until recently, most research on human episodic and semantic memory came from studies of patients with lesion in the medial temporal lobe, and notably the famous patient H.M. [21] thanks to whom we know that remote memories can still be retrieved even without a functional hippocampus and surrounding cortices. However, this patient could only remember the gist of events from his lifetime without any rich episodic details.

Beyond age 7 years, the distribution of memories is assumed to be adultlike in terms of how fast they forget, that is when equal ratios of time passed will result in equal ratios of recall. Importantly, over time, forgetting rate slows so after an initial period of vulnerability, memory traces remain relatively stable over time [22].

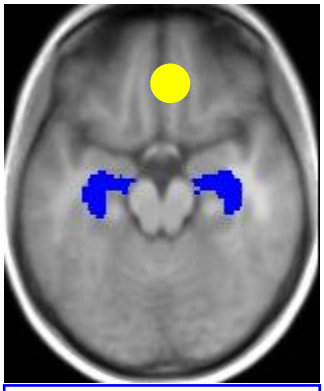
Earliest memories are of events that occurred when the individual was very young; at this time of life, the neural, cognitive, and mnemonic processes that underlie the retention and forgetting of events are not fully formed. Thus, memories of early events are more vulnerable to forgetting.

In childhood, the components of episodic memory capacity develop at different rates. In particular, the spatial and temporal components develop later. For instance, although 4-year-olds can verbally recall factual information learned in an experimental setting, the ability to link this information with the corresponding source (e.g., puppet, experimenter) continues to improve through at least 8 years of age [23].

In one study 4-, 6-, and 8-year-old children recalled several events from the recent past. They were tested for recall of the same events again 1 year later. Children who had been older at the time of the events remembered more of them over the 1-year delay. Specifically, children 4, 6, and 8 years of age at the time of the events remembered 67%, 78%, and 91% of the events 1 year later, when they were 5, 7, and 9 years of age [24]. Indeed, there seems to be **a major shift** in memory retention and consistency of episodic recall **that happens around 5-6 years of age**, when the rate of forgetting begins to slow [22,25].

Thus, current research points that the phenomenon of childhood amnesia is due to the forgetting rate which is faster in younger (pre-school) than in older children.

In addition, childhood memories may be especially vulnerable to forgetting also because their rehearsal seems more coincidental and cue-dependent, resulting in more fragility in the subsequent consolidation and reconsolidation. Young children often recall memories spontaneously and it may be their most dominant way of rehearsing and remembering their personal past [26]. Moreover, some environmental cues, that most adults would definitely notice (i.e., returning to a different room for a test), at times may pass more or less unnoticed by young children. In that sense, children may forget because they wear "different lenses" and the change of context does not serve as a cue to spontaneous recollection (which would reconsolidate and strengthen a memory), leading to forgetting of differences between various autobiographic episodes.



Memory Network

Summary: the making of a memory of your visit today

The processes that give rise to memory in the human brain are not yet fully known. We do know that cellular and system consolidation and reconsolidation are all part of a dynamic, non-linear process that enables us to remember events from our lives even decades later.

We experience the world "episodically" – acquiring knowledge from specific experiences in particular spatial and temporal contexts. These experiences yield representations that allow us to recall both the context-bound episodic experience and the context- free knowledge that can be extracted from the experience. Information is processed simultaneously in multiple representational (sensorial, motor, etc.) systems, such that representations supporting several kinds of "memory" are created in parallel, including episodic and semantic memories. As a result, an episodic memory is

stored in the brain in a “dismembered” form, as bits and pieces represented in distinct brain systems. Thus, recalling an episodic memory involves “reconstruction” – putting together these bits and pieces, accurately or not [27].

As you are walking around the exhibition and making an episodic memory of this event, your cortical systems create various dispersed representations that capture the sensorial elements of this episode. These representations appear to be coded in distributed overlapping patterns that promote generalization and schematization of an episode. This mechanism enables us to distinguish parks from playgrounds and living rooms from kitchens but because it lumps all playgrounds together, inside the schema “playground”. Cortical systems appear to be specialized to extract the semantic features of entities, their statistical regularities, and to form categories and concepts.

Second, a representation is formed within the hippocampal system that captures contextual attributes of the episode, most particularly the spatial context. The hippocampus can represent space very precisely and uses sparse, distributed coding mechanisms that allow it to separate closely related representations. This allows for sharp boundaries between quite similar contexts, between this particular exhibition and all other exhibitions you have seen in your life in this very location.

Then, linkages are instantly made among the various parts of the hippocampal contextual representations, the various parts of the cortical representations, and, finally, the linkages between the hippocampal-contextual representation and the distributed-cortical representations of the elements involved. These depend on your personal life experience, your current goals and affective state and what you are thinking about as you are making this episode.

The next process in the life of a memory, consolidation, could in principle affect each of these representations and linkages. As a result, contextual representations in the hippocampal system, and entity representations in cortical systems, could be strengthened through enhancement of the changes in synaptic connectivity and epigenetic modifications that underlie memory at the cellular level [15].

Creation of new linkages, or variations in the strength of linkages, within either the hippocampal or cortical systems result in memories that can be remembered or not. These linkages will remain critical for recollecting a detailed episodic memory, because the hippocampal representation is an “index” to retrieving the cortical elements as well as to re-represent the specific spatial and temporal contextual information [15,28]. Context also serves as a strong glue to bind together elements that co-occurred in a particular spatial arrangement in a particular episode.

Immediately as an experience unfolds, there are cellular changes that modulate the strength of traces encoding the memory, a process called cellular consolidation. A memory remains labile (that is, open to manipulation) for about 6h after the experience [29]. In the longer run, particularly during sleep, more substantial changes take place at the systems level.

Slow wave sleep repeatedly reactivates the hippocampal and neocortical traces resulting from an episode. During sleep, some selected traces that have been formed during the day will be replayed and consolidated which will lead them to persist and save them from being forgotten. For example, memories that were modulated by novelty, fear and reward are typically prioritized and remembered better for longer [30–32].

Next, synaptic rescaling [33] renormalizes the hippocampal system, leaving only the “chosen” traces above threshold. In the second stage of consolidation, the remaining above-threshold “traces” are replayed to the cortex, forming new associations and strengthening of those ensembles previously

activated as a result of hippocampal replay. Such reactivations act to incorporate information from the new episode into pre-existing cortical stores [34].

Studies in humans suggest that these sleep-dependent changes can lead to a transformation of the initial memory trace from one that is context-specific to one that is more schematic, retaining the gist but not the context. Accordingly, A memory that is never, or rarely, reactivated will not have undergone sufficient waves of synaptic consolidation to allow the formation of multiple distributed traces in the cortex, decreasing its chances to be remembered [17].

Bibliography

1. Moser, M.-B., Rowland, D. C. & Moser, E. I. Place Cells, Grid Cells, and Memory. *Cold Spring Harb. Perspect. Biol.* **7,** a021808 (2015).
2. Hebscher, M., Levine, B. & Gilboa, A. The precuneus and hippocampus contribute to individual differences in the unfolding of spatial representations during episodic autobiographical memory. *Neuropsychologia* **110,** 123–133 (2018).
3. Tulving, E. Episodic and Semantic Memory. *Organ. Mem.* 381–402 (1972).
4. Suzuki, M. *et al.* Male-specific Volume Expansion of the Human Hippocampus during Adolescence. *Cereb. Cortex* **15,** 187–193 (2005).
5. Tonegawa, S., Liu, X., Ramirez, S. & Redondo, R. Memory Engram Cells Have Come of Age. *Neuron* **87,** 918–931 (2015).
6. Horner, A. J., Bisby, J. A., Bush, D., Lin, W.-J. & Burgess, N. Evidence for holistic episodic recollection via hippocampal pattern completion. *Nat. Commun.* **6,** 7462 (2015).
7. Quiroga, R. Q. Declarative Memory Functions. *Nat. Publ. Gr.* **13,** 587–597 (2012).
8. Nader, K. Reconsolidation and the Dynamic Nature of Memory. in *Cold Spring Harbor Perspectives in Biology* **7,** a021782 (2015).
9. Schacter, D. L., Benoit, R. G., De Brigard, F. & Szpunar, K. K. Episodic future thinking and episodic counterfactual thinking: Intersections between memory and decisions. *Neurobiol. Learn. Mem.* **117,** 14–21 (2015).
10. St Jacques, P. L. & Schacter, D. L. Modifying Memory: Selectively Enhancing and Updating Personal Memories for a Museum Tour by Reactivating Them. *Psychol. Sci.* **24,** 537–543 (2013).
11. Moscovitch, M., Cabeza, R., Winocur, G. & Nadel, L. Episodic memory and beyond: The hippocampus and neocortex in transformation. *Annu. Rev. Psychol.* **67,** 105–134 (2016).
12. Forcato, C., Argibay, P. F., Pedreira, M. E. & Maldonado, H. Human reconsolidation does not always occur when a memory is retrieved: The relevance of the reminder structure. *Neurobiol. Learn. Mem.* **91,** 50–57 (2009).
13. Preston, A. R. & Eichenbaum, H. Interplay of hippocampus and prefrontal cortex in memory. *Curr. Biol.* **23,** R764-73 (2013).
14. van Kesteren, M. T. R., Ruiter, D. J., Fernández, G. & Henson, R. N. How schema and novelty augment memory formation. *Trends Neurosci.* **35,** 211–9 (2012).
15. Albo, Z. & Gräff, J. The mysteries of remote memory. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* **373,** 20170029 (2018).
16. Gilboa, A., Rosenbaum, R. S. & Mendelsohn, A. Autobiographical memory: From experiences to brain representations. *Neuropsychologia* **110,** 1–6 (2018).
17. Sekeres, M. J., Moscovitch, M. & Winocur, G. Cognitive Neuroscience of Memory Consolidation. 17–45 (2017). doi:10.1007/978-3-319-45066-7
18. Bonnici, H. M. & Maguire, E. A. Two years later – Revisiting autobiographical memory representations in vmPFC and hippocampus. *Neuropsychologia* **110,** 159–169 (2018).
19. Addis, D. R. & Schacter, D. L. The hippocampus and imagining the future: where do we stand? *Front. Hum. Neurosci.* **5,** 173 (2011).
20. Keven, N., Kurczek, J., Rosenbaum, R. S. & Craver, C. F. Narrative construction is intact in episodic amnesia. *Neuropsychologia* **110,** 104–112 (2018).
21. Squire, L. R. & Wixted, J. T. The cognitive neuroscience of human memory since H.M. *Annu. Rev. Neurosci.* **34,**

259–88 (2011).

22. Bauer, P. J. & Larkina, M. Childhood amnesia in the making: Different distributions of autobiographical memories in children and adults. *J. Exp. Psychol. Gen.* **143,** 597–611 (2014).

23. Cuevas, K., Rajan, V., Morasch, K. C. & Bell, M. A. Episodic memory and future thinking during early childhood: Linking the past and future. *Dev. Psychobiol.* **57,** 552–565 (2015).

24. Morris, G., Baker-Ward, L. & Bauer, P. J. What remains of that day: The survival of children's autobiographical memories across time. *Appl. Cogn. Psychol.* **24,** 527–544 (2010).

25. Peterson, C., Hallett, D. & Compton-Gillingham, C. Childhood Amnesia in Children: A Prospective Study Across Eight Years. *Child Dev.* **0,** 1–15 (2017).

26. Sonne, T., Kingo, O. S., Berntsen, D. & Krøjgaard, P. Thirty-five-month-old children have spontaneous memories despite change of context for retrieval. *Memory* **8211,** 1–11 (2017).

27. Nadel, L., Hupbach, a., Gomez, R. & Newman-Smith, K. Memory formation, consolidation and transformation. *Neurosci. Biobehav. Rev.* **36,** 1640–1645 (2012).

28. Moscovitch, M., Nadel, L., Winocur, G., Gilboa, A. & Rosenbaum, R. S. The cognitive neuroscience of remote episodic, semantic and spatial memory. *Curr. Opin. Neurobiol.* **16,** 179–190 (2006).

29. Schiller, D. *et al.* Preventing the return of fear in humans using reconsolidation update mechanisms. *Nature* **463,** 49–53 (2010).

30. Roozendaal, B. & McGaugh, J. L. Memory modulation. *Behav. Neurosci.* **125,** 797–824 (2011).

31. Miendlarzewska, E. A., Bavelier, D. & Schwartz, S. Influence of reward motivation on human declarative memory. *Neurosci. Biobehav. Rev.* **61,** 156–176 (2016).

32. Takeuchi, T. *et al.* Locus coeruleus and dopaminergic consolidation of everyday memory. *Nature* **537,** 357–362 (2016).

33. Tononi, G. & Cirelli, C. Sleep and the price of plasticity: from synaptic and cellular homeostasis to memory consolidation and integration. *Neuron* **81,** 12–34 (2014).

34. Diekelmann, S. & Born, J. The memory function of sleep. *Nat. Rev. Neurosci.* **11,** 114–26 (2010).