

It's In My Eyes, but It Doesn't Look that Way to Me

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In this issue of *Neuron*, Hannula and Ranganath provide striking evidence that hippocampal activity predicts eye movements that reveal memory for the past even when participants' overt memory decisions are in error. Their findings bear on an ongoing debate about the relationship between mnemonic awareness and hippocampal function.

Do our eyes reveal more than we are able to disclose? Consider for a moment the following scenario: a witness to a robbery is confronted with a line up and asked to single out the culprit. The witness, feeling unsure, declares he is unable to identify the miscreant, and yet his eyes tell a different story, being drawn unknowingly to the perpetrator's face, revealing a memory of the past that the witness cannot consciously report. In this issue of *Neuron*, Hannula and Ranganath (2009) demonstrate that the hippocampus underpins such eye-movement phenomena, providing a tantalizing glimpse into a mnemonic milieu apparently beyond awareness.

The idea that unconscious (i.e., implicit or nondeclarative) memories exert powerful influences on behavior and depend on distinct neural mechanisms from consciously accessible (i.e., explicit or declarative) memories has a long history. Over the past few decades, extensive evidence has established the critical role of the hippocampus and surrounding medial temporal lobe (MTL) structures in conscious memory for life's events. Moreover, repeated demonstration that impaired conscious recollection following hippocampal damage is accompanied by preserved skill learning, habit learning, and priming—all forms of memory that can unconsciously shape behavior—has motivated the hypothesis that the hippocampus plays a selective role in conscious memory for facts and events (Schacter, 1987; Squire et al., 2004).

The view that hippocampal mnemonic function is intimately linked to awareness, while dominant, has recently been challenged by a handful of empirical findings suggesting that amnesic patients with hippocampal lesions also show deficits on tasks that putatively assess implicit memory for the relations between event elements (Chun and Phelps, 1999; Ryan et al., 2000). For instance, Ryan et al. (2000) demonstrated that amnesic patients fail to direct their gaze to parts of a previously studied scene that contain novel relations between scene elements, whereas control participants exhibit such eye-movement phenomena even when they lack awareness that the scene has changed across repetitions. These and other observations, while controversial in their own right (Manns and Squire, 2001; Preston and Gabrieli, 2008; Smith et al., 2006), offer support for an alternative view of hippocampal mnemonic function, namely that the hippocampus is critical for relational memory—i.e., memory for the relations between the individual elements of an experience—and contributes to performance irrespective of whether the participant is aware or unaware that relational knowledge has been retrieved (Cohen and Eichenbaum, 1993).

Hannula and Ranganath offer a fresh perspective on this debate, by combining eye-movement recordings with functional MRI to generate a rich data set linking neural processes to behavioral expressions of memory retrieval. In their experiment, healthy volunteers first encoded pictures of individual faces superimposed

on individual scenes. Subsequently, during test trials, participants were initially presented with a studied scene and instructed to remember the face with which it had previously been paired, and then, after a delay, were asked to select the matching face from a three-face choice array (the distractors had been previously encountered with other scenes at study). Critically, eye movements were recorded during test trials, enabling assessment of whether participants' gazes were drawn to the matching face in the array even before they explicitly reported their memory judgment, and perhaps even when their subsequent choice was erroneous. In this way, the authors sought to (1) demonstrate the influence of relational memory on eye movements and reveal their neural origin and (2) determine whether such relational eye-movement effects (hereafter termed "REMES") are expressed even when subjective reports are erroneous, which might suggest that REMES are a manifestation of unconscious relational memory.

To accomplish their first aim, the authors categorized test trials according to whether participants disproportionately viewed either the matching face (DMP trials) or one of the distractor faces (DNMP trials). What they found was that, as early as 500–1000 ms after the onset of the face array, viewing times of the matching face on DMP trials were significantly greater than of the selected face on DNMP trials, consistent with an influence of relational memory retrieval during DMP trials. Furthermore, neural activity

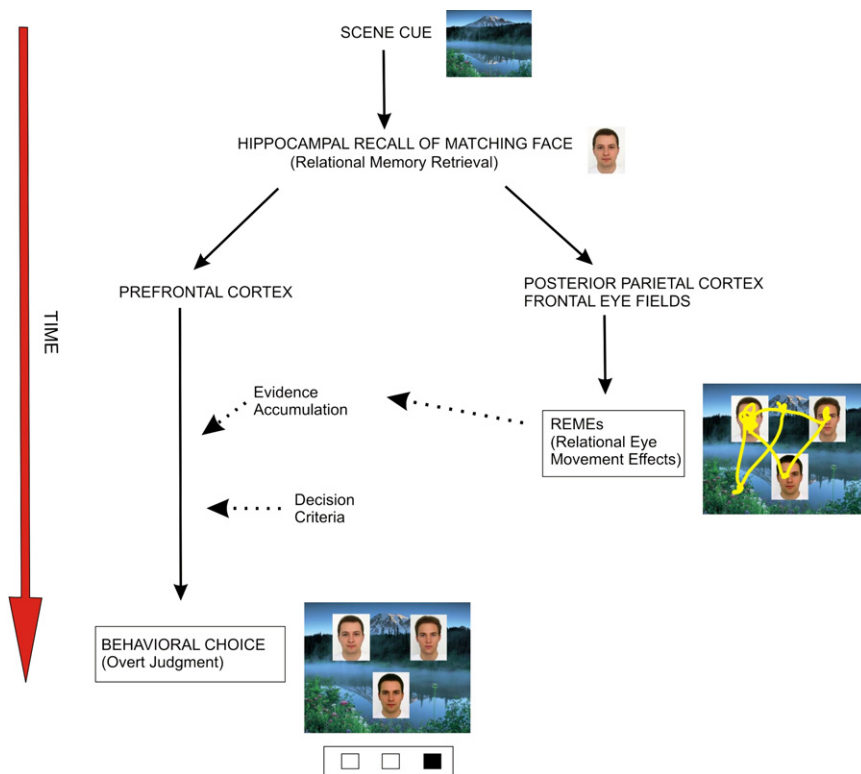


Figure 1. Schematic Linking Hippocampal Relational Memory Retrieval to REME Expression and Overt Judgments

in the hippocampus and several adjacent MTL structures was significantly greater during DMP trials as compared to DNMP trials, suggesting that these brain regions support relational memory retrieval during the scene cue period that directs participants' gaze to the matching face during the choice array phase.

To address their second aim, the authors next asked whether their two behavioral measures (REMEs versus choice accuracy) could be dissociated—that is, is relational memory evident in eye-movement behavior even when the participant fails to select the matching face? Addressing this question was far from straightforward, because, perhaps unsurprisingly, the two behavioral indices were highly correlated, with memory accuracy being markedly higher on DMP (83%) than on DNMP (35%) trials. To gain leverage on this issue, the authors therefore focused on trials where the participant's subsequent memory decision during the choice array was incorrect, median splitting incorrect trials into high- and low-viewing trials depending on time

spent viewing the matching—but ultimately not selected—face. Strikingly, activation in the hippocampus during the preceding scene cue phase again predicted longer subsequent viewing of the matching face, implying that successful relational memory retrieval is evident in eye-movement behavior even when the participant's overt memory judgment is incorrect.

Given the observation that activity in the hippocampus was intimately linked to the expression of REMEs irrespective of memory accuracy, one might wonder whether accurate memory decisions were associated with activity in other neural structures. Indeed, in a final analysis, Hannula and Ranganath observed that activity in regions within lateral prefrontal cortex (PFC) was modulated by memory judgment accuracy, being greater on correct versus incorrect trials. Further, lateral PFC showed increased functional coupling with the hippocampus during correct versus incorrect trials, suggesting that relational memory retrieval *per se* relies on the hippocampus, but accurate

overt relational memory decisions necessitate interactions between MTL structures and the PFC.

While previous studies implicating the hippocampus in the generation of unaware memory-guided eye movements have been challenged (Smith et al., 2006), the current study provides compelling evidence demonstrating that neural activity in the hippocampus predicts REME expression, preceding their appearance by as much as several seconds. Perhaps even more intriguingly, the observation that hippocampal activity also predicted REME expression even when overt memory decisions were erroneous raises the possibility that REMEs and explicit relational memory judgments index the outputs of two anatomically segregated pathways that drive distinct aspects of behavior, the former perhaps generated in the absence of conscious awareness, and the latter reflecting explicit goal-directed behavior (see Figure 1). As such, Hannula and Ranganath's data dovetail with recent work showing that hippocampal activity can distinguish the old/new status of stimuli, even when participants' recognition judgments fail to do so (Daselaar et al., 2006; Kirwan et al., 2009).

Interestingly, Hannula and Ranganath eschew claims that the eye-movement effects they observe are manifestations of implicit memory, preferring to frame their results in terms of a dissociation between different behavioral indices of relational memory retrieval. The authors are likely wise to do so, as a strong conclusion that the present REMEs reflect unconscious (unaware) memory would appear somewhat premature given the data. Rather, while the observed dissociation between REME expression and choice behavior is certainly consistent with the conclusion that REMEs reflect unaware relational memory, an alternative account remains viable. Namely, it is possible that participants were in fact conscious of the mnemonic status of the match face at the time of prolonged viewing (i.e., the 500–1000 ms period) but were unable to or chose not to act on this information 1 s later when the memory decision was required. Why might this have been the case? One possibility is that other cognitive processes intervene between the occurrence of REMEs and

the memory judgments, which result in participants deviating from their seemingly accurate course to ultimately selecting an erroneous face (see Figure 1). According to this perspective, REMEs may reflect early emerging, and perhaps relatively pure, signatures of memory retrieval that are overridden by the subsequent accumulation of evidence from other sources (e.g., from the consideration of alternative options) which eventually determine the participant's ultimate behavioral choice (Gold and Shadlen, 2007).

The interpretative caution shown by Hannula and Ranganath, as well as past challenges in convincingly documenting the existence of implicit relational memory, begs the question: What kind of evidence would be required to demonstrate that participants were truly unaware at the time of relational eye-movement expression? One strategy for tackling this issue might be to modify the parameters of the task, so that participants were forced to make speeded memory judgments during the same temporal window as REME expression. If it were possible to drive speeded response accuracy to demonstrably chance levels, perhaps by reducing the temporal gap between scene cue and face array to a few hundred milliseconds, the continued expression of REMEs would provide more compelling evidence that participants lack awareness of the match status of the target face at time of REME expression. Even if this manipulation failed to reduce response accuracy to chance, the existence of REMEs on trials where participants made cotemporaneous incorrect choices would still offer some support for the contention that REMEs reflect implicit memory. However, it is worth noting that, while speeded responses, in combination with prior work (Ryan et al., 2000), may provide evidence to support the claim that REMEs are a manifestation of implicit (unaware) memory, providing definitive evidence that subjects truly lack awareness is notoriously difficult (Shanks and St. John, 1994).

On the other hand, if the proposed experimental manipulations failed to yield a dissociation between REMEs and choice accuracy, this would challenge the notion that REMEs occur outside awareness. Instead, this would imply that Hannula and Ranganath's participants may have been conscious of the match status of targets at the time of REMEs, but were subsequently led astray during incorrect trials through the operation of intervening cognitive processes (see Figure 1). One way to provide evidence for this account might be to have participants declare their choices at two time points: first at the time of REME expression and then a few seconds later as in the current experiment. If the choice data reveal that participants sometimes select the correct matching face at time of REME expression, but subsequently render an incorrect response, this would favor the hypothesis that REMEs and conscious awareness are intimately linked.

While the relationship between REMEs and implicit memory remains uncertain, the study by Hannula and Ranganath highlights the utility of eye-movement data as an alternative, and potentially more sensitive, behavioral assay of memory retrieval and hippocampal function. As the authors point out, the wider use of eye-movement measures is also likely to be a fruitful approach with which to explore hippocampal function in a range of settings where memory judgments are troublesome to obtain (e.g., animals, infants). REMEs may also prove a purer assay of memory, as compared to explicit memory reports, which can have the added complication of tending to change the way in which participants encode and retrieve information. As such, REMEs complement an emerging literature on the neural signals of novelty/familiarity, which are readily measured in tasks lacking explicit demands to learn and remember (Kumaran and Maguire, 2009). Moreover, eye-movement phenomena provide a temporally precise measure that indexes the evolution of relational memory expression from perception to

action, a process that may depend on interactions between the MTL and PFC as the authors' findings suggest.

Survival in an ever-changing world depends on the capacity to rapidly express memory. That eye movements may be guided by memory for the past is no longer surprising. That hippocampal relational memory signals may underpin what the eyes "know," even when conscious retrieval fails, is what intrigues. Continued exploration of the link between eye movements and memory may eventually resolve key debates about the hippocampus's function and perhaps even the very nature of unconscious memory itself.

REFERENCES

- Chun, M.M., and Phelps, E.A. (1999). *Nat. Neurosci.* 2, 844–847.
- Cohen, N.J., and Eichenbaum, H. (1993). *Memory, Amnesia and the Hippocampal System* (Cambridge, MA: MIT Press).
- Daselaar, S.M., Fleck, M.S., Prince, S.E., and Cabeza, R. (2006). *J. Neurosci.* 26, 5835–5839.
- Gold, J.I., and Shadlen, M.N. (2007). *Annu. Rev. Neurosci.* 30, 535–574.
- Hannula, D.E., and Ranganath, C. (2009). *Neuron* 63, this issue, 592–599.
- Kirwan, C.B., Shrago, Y., and Squire, L.R. (2009). *Proc. Natl. Acad. Sci. USA* 106, 1417–1421.
- Kumaran, D., and Maguire, E.A. (2009). *Trends Cogn. Sci.* 13, 47–54.
- Manns, J.R., and Squire, L.R. (2001). *Hippocampus* 11, 776–782.
- Preston, A.R., and Gabrieli, J.D. (2008). *Cereb. Cortex* 18, 2192–2207.
- Ryan, J.D., Althoff, R.R., Whitlow, S., and Cohen, N.J. (2000). *Psychol. Sci.* 11, 454–461.
- Schacter, D.L. (1987). *J. Exp. Psychol. Learn. Mem. Cogn.* 13, 501–518.
- Shanks, D.R., and St. John, M.F. (1994). *Behav. Brain Sci.* 17, 367–447.
- Smith, C.N., Hopkins, R.O., and Squire, L.R. (2006). *J. Neurosci.* 26, 11304–11312.
- Squire, L.R., Stark, C.E., and Clark, R.E. (2004). *Annu. Rev. Neurosci.* 27, 279–306.