Flexible recoding of visual input for memory storage

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Working memory enables us to maintain relevant past information for future behavior. In this issue of *Neuron*, Kwak and Curtis (2022) demonstrate that early visual areas do not simply maintain but flexibly recode sensory percepts into mnemonic codes containing goal-relevant information.

Working memory is the capacity to maintain past sensory percepts over relatively short periods of time. This ability allows us to stitch together sensory inputs into meaningful representations that persist over discontinuities in the input stream. As such, it liberates us from being trapped in the present moment and enables us to think about the past and plan for the future.

The question of where in the brain mnemonic representations of sensation are stored has triggered substantial interest in neuroscience. Research has revealed that higher-order regions, such as the prefrontal and posterior parietal cortices, are essential for maintaining information in mind. For instance, patients with prefrontal damage have difficulties in maintaining and manipulating information in memory (Baddeley, 1986; Chao and Knight, 1998). Further support for the role of higher-order regions comes from neuroimaging and electrophysiological research demonstrating that activity in prefrontal regions is sustained over timescales longer than sensory presentation, making it suitable to store memory representations (Hasson et al., 2015). While the importance of higher-order regions in working memory is undisputed, the role of early sensory regions has remained more elusive. Some have advocated that early sensory regions play a critical role in memory storage (Pasternak and Greenlee, 2005; Harrison and Tong, 2009). The key tenet of this ''sensory storage'' account is that the same sensory regions involved in processing the input are also recruited to maintain the sensation in memory. Put differently, working memory is thought to be substantiated by prolonging the representation formed during the initial encoding. This may enable people to remember specific features of stimuli, such as the orientation of a grating, with high specificity, even when such features are difficult to verbalize. Such stimuli may be less amenable to an abstract code in higher-order regions, and could thus be better stored by neurons in early visual regions that exhibit selective tuning to low-level features. The evidence for sensory storage during visual working memory has been, however, somewhat mixed. While many studies have demonstrated that early visual areas maintain stimulus-specific information even when the stimulus is no longer in view (e.g., Harrison and Tong, 2009), others have shown that the mnemonic code of a stimulus often differs from the stimulus-evoked activation in those regions (Bettencourt and Xu, 2016; Rademaker et al., 2019). A possibly even bigger challenge for the sensory storage account is that of interference: storing the information within early sensory regions could make memories susceptible to overwriting by the continuous influx of information; yet everyday vision seems to be resilient against such distractors. This has led some to question the role of sensory regions in working memory and, rather, advocate that associative regions alone could act as the storage site of memories (Xu, 2017). The current investigation by Kwak and Curtis (2022) adds a new and interesting twist to this debate, which could potentially resolve some of the aforementioned issues. They demonstrate that the early visual cortex contains stimulus-specific information in memory. However, these regions do not simply maintain a faithful representation of the input in the same format as during initial viewing. Instead, the representation is flexibly recoded into a more useful format that can support future behavior.

The study is set up to test the hypothesis that mnemonic representations of visual features differ from perceptual representations in early visual areas. To address this, the authors present human volunteers with a delayed working memory task on two types of stimuli: oriented gratings and moving dots (Figure 1). Individuals are asked to remember the orientation of the stimuli as they are removed from the screen. Following a delay period, a probe appears, which participants have to re-orient to match the orientation of dots or gratings presented initially. Throughout the task, participants' brain activity is measured using fMRI. How might we expect the brain to represent these visual stimuli during the delay? One possibility is that the visual working memory is primarily instantiated through higher-order regions that keep an abstract, yet stimulus-specific, representation of these inputs, for instance by maintaining a verbal code of the relevant feature (i.e. remembering the gratings or dots are oriented ''rightwards''—Figure 1), while the primary visual cortex (V1) does not necessarily contain any information about the stimulus in the delay period. In contrast, if sensory areas are responsible for storing the visual working memory, the memory code in V1 should match the sensory code elicited by the stimuli initially. Specifically, the code for the gratings should remain ''grating-like'' and the code for the dot motion stimuli

"dot-like." The obtained findings differed from both predictions—during the delay period, V1 activity remained stimulus specific, but the format of the code changed. The representation was no longer specific to each stimulus (dots or gratings) but instead became reformatted into a line-like representation for both visual features. This was demonstrated by a sophisticated set of analysis. First, the orientation of stimuli was decodable from the delay activity across stimuli sets (i.e. from gratings to dot motion and vice versa). Critically, this cross-decoding was not achievable for activity elicited during the initial viewing, indicating that the representation across stimuli sets became more alike during the delay period because of the similar task demands (reorienting the stimuli) and not because of perceptual similarity. Second, reconstructing the spatial activity profile during the delay period revealed a line-like format for both stimuli sets, which was not (or less) present during the initial encoding. Thus, V1 activity reflects recoding of sensory percepts into a format that captures the goal-relevant features. In this task, a line is well-suited to efficiently remember the orientation of the stimuli while dropping the unnecessary perceptual details of gratings or dots from memory. The exciting aspect of this study is the demonstration that even early visual regions can reformat their sensation-elicited activity into a memory code better suited to support task demands. The findings are also in line with the notion that the early visual cortex serves as a cognitive "blackboard" for read and write operations by higher visual and associative areas (Roelfsema and de Lange 2016).

The study by Kwak and Curtis raises several new lines of inquiry. One important question concerns how task demands influence the mnemonic code in sensory areas. If the task would not
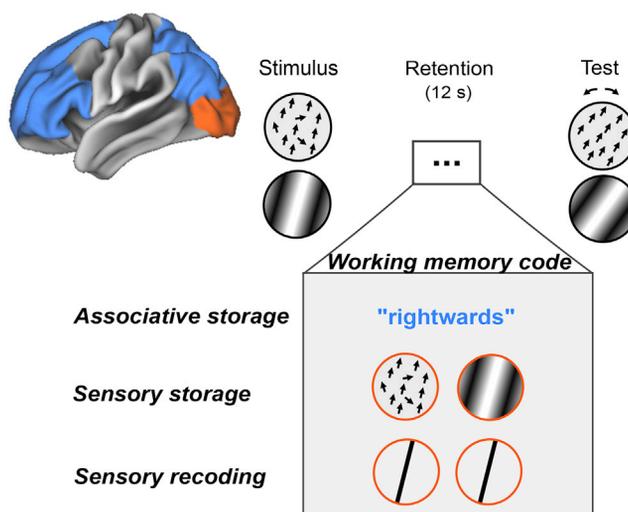
Figure 1. Task and predictions about representational format of visual working memory
Participants were presented with either a random dot motion kinematogram or an oriented grating (in separate blocks). After a retention interval where the stimuli were removed, a probe was presented, which participants had to orient to match the initial presentation. If visual working memories are stored in associative cortex, an abstract code should be present during maintenance in prefrontal and parietal regions, but early visual regions should not maintain a memory of the stimuli. If visual working memories are stored in visual cortex, early sensory regions should contain a memory code of each stimulus, matching the perceptual code. The authors here find that the early sensory regions contain a memory code of the stimulus, but the code is recoded from perception into the same line-like representation for both types of stimuli.

have required participants to actively orient a probe to report working memory, but simply to discriminate the working memory from a test stimulus (e.g. is the grating oriented clockwise or counterclockwise relative to initial encoding), would the memory code still be recoded into a low-dimensional line? It appears plausible that the recoding of visual input in working memory is a flexible process that can be strategically employed in line with an observer's goals.

It should also be mentioned that while the present investigation focusses on the role of early sensory areas in working memory, this should not be taken as an indication that the early sensory areas support behavior per se. There are multiple other codes that exist in parallel across distributed brain regions—such as a verbal code for rehearsal or a motor code preparing the behavioral response. Future research is needed to better relate these distributed mnemonic codes to each other and to understand how they underpin behavior.

Finally, in the present investigation, there was no visual stimulation during the entire 12 s of the retention period, which is very unlike everyday vision when we are constantly bombarded with information. Thus, it remains to be seen how sensory areas can keep an abstract memory representation while responding also to the new perceptual demands. Interestingly, the notion of sensory recoding could serve as an elegant solution for the thorny issue of interference: it could enable preservation of the relevant information, while also processing the new stimuli in full detail. How such multiple codes can coexist, transform, and communicate across initial encoding, delay, and retrieval period raises intriguing questions to test in the future. Altogether, the new investigation by Kwak and Curtis may spearhead a new wave of exciting research on the old question of how sensory regions store perceptions to support real-world visual cognition.

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Once is enough for hippocampal replay

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In this issue of *Neuron*, Berners-Lee et al. (2022) reveal how neural dynamics in the hippocampus change after a single experience, offering a candidate mechanism for how hippocampal plasticity supports episodic memory.

Despite lives immersed in change, we manage to extract and generalize commonalities to make sense of the causal structure of our world. To do so, we must relate memories of moments separated in time, each lived once only. How does the brain accommodate such "one trial learning," and how can new information be assimilated when the core aspects of an experience are repeated? These problems are not simple, for, as Louis MacNiece wrote in *Variation on Heraclitus*, "One cannot live in the same room twice."

Berners-Lee and colleagues tackle these profound questions in their most recent article on how hippocampal dynamics change after rats explore a new physical space (Berners-Lee et al., 2022). They targeted the hippocampus due to this region's critical role for the encoding, storage, and retrieval of episodic memories, those that form the record of our lived experience at a past time and place. Electrophysiological studies have shown that, among other world variables, hippocampal firing correlates with the location of the subject, such that different groups of neurons show place field activity in different locations. Moving across a room causes a sequence of neural ensembles to be active, because different neurons fire in different locations and

because the traversal of space must unfold over time. These neural sequences are somehow learned and later "replayed" during sharp wave ripples (SPW-Rs; Wilson and McNaughton, 1994), which are oscillatory population bursts generated by the intrinsic circuitry of area CA1 (Buzsaki, 2015).

One challenge in studying the neural basis for episodic memory is that these are the memories of events that take place only once. Neurons are noisy, and often animals must be trained to do the same behavior with tens and sometimes hundreds of repetitions to extract meaningful neural correlates. Given these constraints, several strategies were needed to study how a single experience could leave its mark on neural dynamics.

Absent the ability to study trial-averaged neural activity, Berners-Lee et al. adopted the high-density tetrode recordings that have powered much of the work from the Foster lab, allowing for the simultaneous recordings from over 200 CA1 neurons. Ensemble recordings were then analyzed with a sophisticated set of statistical methods that were developed by the same group across several influential reports. These tools are designed to parse whether observed replay sequences differ from stochastic noise and

to measure how replay structure is entrained to the oscillations in which the events are embedded. Finally, in a testament to the growing open science movement, this manuscript included data from seven prior studies (six from the Foster group, one from the Buzsaki lab).

The critical observation made by Berners-Lee et al. was that rats needed to traverse a location just once for significant replay to emerge; somehow that single experience was sufficient to change the replay content for the next hour. The authors arrived at this conclusion through Bayesian decoding analysis of population bursts to reconstruct putative replay paths. By shuffling the spike timing, candidate replay events could be compared against random null distributions. Before track exposure, candidate events looked like the shuffled null across many possible definitions of which population bursts should count as a replay; there are many free parameters in this type of analysis, and such parameter sweeps are needed when we lack the ground truth for how a replay event should be defined. After a single track exposure, replay was confirmed across more of the parameter space used to define which spike patterns constitute a candidate event.