stimulation, Blanes cells respond with pronounced after-depolarizations that last only a few seconds. Under these conditions, Blanes cells could mediate short-term reductions in lateral inhibition or could potentially have the opposite effect. Granule cells can engage in "classic" T-type calcium channel-mediated depolarizations that are enhanced by prior hyperpolarization (Egger et al., 2003). By providing transient hyperpolarizations onto granule cells, GABAergic inputs from Blanes cells could indirectly augment granule cell excitation, leading to enhanced lateral inhibition or synchrony.

Among the remaining questions about these interesting neurons, one of the most fundamental is related to the strength of the inhibitory drive provided by Blanes cells. There is little information about the number of Blanes cells in the bulb, and there also remain several other poorly characterized classes of short-axon interneurons in the bulb that could subserve functions similar to Blanes cells (see, for example, Price and Powell, 1970; Schneider and Macrides, 1978). The most intriguing experiment in the present study that suggests that Blanes cells have significant action is one in which granule cell spiking is shown to be reduced by electrical stimulation in the granule cell layer, with an effect that is reversed by a $GABA_A$ receptor blocker. Future studies will need to resolve whether this granule cell suppression is due to Blanes cells or other GABAergic interneurons. An additional issue is related to the anatomy of Blanes cells, specifically the length of their axon. The axon length is important, since space is of critical concern for olfactory bulb processing. Anatomical studies have shown that mitral cells are organized into discrete functional glomerular "modules" that correspond to single odorant receptors, with each module being a few hundred microns in diameter. Blanes cells with short axons could mediate disinhibition among mitral cells of the same glomerular module or between nearby modules, whereas Blanes cells with long axons could mediate disinhibition between widely separated modules. Because an odor is known to activate widely separated glomeruli (Rubin and Katz, 1999; Korsching, 2002), Blanes cells with long axons could have unique functions in coordinating different odor-activated modules. The combination of detailed anatomical studies together with novel functional methods hopefully will resolve some of these issues.

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Attending to Remember and Remembering to Attend

Attention and memory are intimately linked. Two functional imaging studies in this issue of *Neuron* provide novel evidence for this powerful, reciprocal relationship. Turk-Browne and colleagues report that attention simultaneously facilitates the formation of both implicit and explicit memories, while Summerfield and colleagues demonstrate that memory for the past can guide the allocation of attention in the present. Together, these elegant studies reveal bidirectional interactions between attention and memory.

In 1759, the English poet Samuel Johnson famously noted that "the true art of memory is the art of attention," capturing a central tenant of the workings of memory: the encoding of an experience into memory is greatly influenced by how attention is allocated during the experience. For example, everyone has likely experienced the social embarrassment of failing to remember the name of a new acquaintance met but moments ago at a party. Often these awkward moments reflect a failure to encode the person's name because at the time of introduction one's attention was distracted by other thoughts or stimuli in the environment. Consistent with such anecdotes, extensive behavioral research indicates that divided attention at the time of learning results in diminished subsequent memory for an event relative to when attention is fully dedicated during encoding. This effect of attention appears to generalize across memory systems, as attention influences learning within the explicit (declarative) memory system that supports conscious remembering of events (e.g., Craik et al., 1996), as well as within implicit (nondeclarative) memory systems that allow the past to nonconsciously influence subsequent perception and action (e.g., Mulligan, 1998).

While attention is critically important for effective learning, the crosstalk between attention and memory is a two-way street: memory for the past can serve to guide how we allocate attention in the present. For example, perceiving the action during sporting events is often a challenge for viewers who lack knowledge of a sport, whereas fans can rely on their memories of regular, highly predictable sequences of action to selectively attend to portions of the unfolding visual input. Such memory-guided allocation of visuospatial attention increases the likelihood that the fan will perceive a developing backdoor cut, a catcher's sign to the

pitcher, or a cornerback's jam. Consistent with this perspective, emerging behavioral and neuropsychological evidence indicates that explicit and implicit memories derived from past experience can provide predictive information about which aspects of an environment or stimulus are likely to be relevant. In so doing, memory can serve to modulate the allocation of selective attention, facilitating perception of current stimuli (e.g., Chun and Phelps, 1999; Moores et al., 2003).

Given that attention and memory are intimately linked, understanding the cognitive and neural mechanisms underlying each of these abilities will partially depend on specifying when and how these systems interact. In this issue of *Neuron*, two functional magnetic resonance imaging (fMRI) studies provide compelling new data that complement and extend prior behavioral observations of the bidirectional dynamic between attention and memory. These important new studies advance understanding of how attention to a stimulus can simultaneously influence the encoding of implicit and explicit memories (Turk-Browne et al., 2006) and how memories, once encoded, can provide predictive information that modulates the orienting of attention (Summerfield et al., 2006).

Implicit and explicit memory systems depend on separable cognitive and neural architectures, permitting their independent operation. Given the dissociable nature of these two forms of memory, it has remained unclear whether the formation of implicit and of explicit memories deriving from an experience are simultaneously influenced by common processing factors, such as attention. To address this central question, Turk-Browne et al. (2006) cleverly combined a repetition priming paradigm that reveals behavioral and neural correlates of implicit memory with a subsequent memory analysis that reveals neural correlates of explicit encoding. In the repetition priming paradigm, participants were scanned using event-related fMRI while classifying individual novel and repeated photographs as depicting either an indoor or outdoor scene. During the scan, implicit memory was measured by *behavioral priming*—a reduction in reaction time to classify repeated (second) compared to novel (first) presentations of items—and by *neural attenuation*—a reduction in neural activation when classifying repeated compared to novel items (e.g., Grill-Spector et al., 2006). Approximately 15 min after the fMRI session, participants received an unexpected recognition memory test for the scenes that they had classified. Their performance on this test provided a measure of subsequent explicit memory for each of the items encountered during scanning, a measure that was used to back-sort the fMRI encoding data into items subsequently explicitly remembered and items subsequently forgotten (e.g., Paller and Wagner, 2002).

Sorting the fMRI encoding trials according to explicit memory status revealed three striking patterns. First, the magnitude of behavioral priming during repeated classification of a scene was robust for scenes later explicitly remembered but was markedly reduced for scenes subsequently forgotten. To the extent that this behavioral facilitation reflects implicit memory arising from the prior encounter with the scene, then this finding reveals that effective implicit memory formation (marked

by behavioral priming) correlates with effective explicit memory formation (marked by subsequent explicit remembering). Second, experience-dependent neural attenuation within the "parahippocampal place area" (PPA), a region in posterior parahippocampal cortex that is differentially responsive during scene perception, was also greater for scenes that were subsequently explicitly remembered than for scenes subsequently forgotten. That is, the cortical plasticity associated with implicit memory appears to be modulated by factors that also influence explicit encoding. Finally, Turk-Browne et al. observed that the level of tonic neural activity immediately prior to the first presentation of a scene, which may signal the level of attention then allocated during scene encoding, was reliably greater for subsequently remembered versus forgotten items. Collectively, these results suggest that the formation of implicit and explicit memories during an experience are simultaneously affected by common factors, with attention being one such factor.

Whereas Turk-Browne et al. (2006) provide new evidence that attention concurrently influences learning within multiple memory systems, Summerfield et al. (2006) address how memory, in turn, can guide attention. Using event-related fMRI, they compared memory-guided attentional orienting to more traditional exogenously cued attentional orienting. Prior to scanning, participants were pre-trained on a set of complex visual scenes, two-thirds of which contained a target object. During training, each scene was encountered five times, ensuring that participants were familiar with this set of scenes and with the target object's location in those scenes that contained a target. Following training, participants were scanned while performing two target detection tasks. In the exogenously cued *visual-orienting task*, participants detected whether or not the target object was present within untrained (novel) scenes. In this task, on some trials a peripheral visual cue served to guide the allocation of attention to a particular location within the scene where the target might appear. By contrast, in the *memory-orienting task*, participants detected whether or not the target was present within the pre-trained, familiar scenes, thus allowing participants' memory to guide their attention to the target's expected location in the scene.

Within this sophisticated experimental design, Summerfield et al. (2006) obtained two important outcomes. First, participants were significantly faster at detecting the target object within a familiar scene when prior experience provided a memory-based expectation about the object's location compared to when there was no memorized location for the object. Strikingly, this behavioral benefit of memory-based attentional orienting was greater than the benefit accrued when attentional orienting was informed by a peripheral visual cue. Thus, not only can memory flexibly and efficiently guide selective attention to enhance the perception of objects embedded in complex visual contexts, but memory may sometimes be a superior predictive cue than transient perceptual events. Second, at the neural level, fMRI revealed that memory-guided attention recruits many of the same parietal-frontal areas—intraparietal sulcus, frontal eye fields, and cingulate cortex—that are engaged when visuospatial attention is exogenously

cued by a visual stimulus. However, in contrast to exogenously cued attentional orienting, memory-guided orienting was further accompanied by activation in the hippocampus, consistent with the known role of this structure in encoding and retrieving knowledge about the relations among stimuli, such as the relations between objects in space. Summerfield et al. observed that the hippocampus was the only structure in which activation levels correlated with the magnitude of the behavioral benefit arising from predictive memory-orienting versus visual-orienting. This finding complements prior data demonstrating experience-dependent plasticity within hippocampus that can serve as a predictive code for subsequent behavior (e.g., Mehta, 2001). Accordingly, Summerfield et al.'s data document a dynamic interplay between memory and attention, wherein neural regions critical for relational memory provide predictive information about the probable location of relevant stimuli and thus guide engagement of the parietal-frontal attention network to selectively attend to the predicted location. The behavioral consequence of this memory-attention interaction is enhanced perception of objects appearing in predicted locations.

Given the common impact of attention on implicit and explicit memory observed by Turk-Browne et al. (2006), a natural question is whether the memory-guided attentional orienting observed by Summerfield et al. (2006) reflects the predictive power of explicit memory, of implicit memory, or both. These authors emphasize that their data could reflect the efficacy of explicit and/or implicit memory in driving attention. On the one hand, the hippocampus is clearly essential for explicit (declarative) memory, raising the possibility that the observed hippocampal activation during memory-orienting reflects the retrieval of explicit knowledge. On the other, the observed consequences of memory in yielding attentional biases were apparent with as little as 100 ms between scene and target onset, which raises the possibility that they reflect the rapid expression of implicit knowledge. Moreover, while controversial, recent data from amnesic patients with medial temporal lobe (MTL) damage suggest (1) that the MTL may also be important for acquiring implicit (nondeclarative) contextual information that facilitates visual search (Chun and Phelps, 1999) and (2) that experience-dependent changes in eye-tracking when viewing complex visual scenes, which may reflect nonconscious knowledge about the relations between objects in space, depend on the integrity of the MTL (Ryan and Cohen, 2004). Accordingly, an important direction for future research is specifying the exact nature of Summerfield et al.'s reported mnemonic influences on attention. Moreover, while Summerfield et al.'s findings suggest that the hippocampus is central for the observed memory-orienting effects, other data suggest that parahippocampal gyrus, and perhaps lateral temporal cortex, is particularly critical for memory-guided visual search (Manns and Squire, 2001). Thus, the dependence of the present memory-attention crosstalk on hippocampus proper versus parahippocampal gyrus awaits examination of the integrity of such mnemonic biases in amnesic patients with damage to different components of the MTL circuit.

While the two experiments highlighted here illustrate mutual benefits between attention and memory, interactions between these systems can also carry costs. Since accurate memory-based prediction can facilitate perception, a likely corollary is that when our predictions are violated we suffer a cost. Within the Summerfield et al. (2006) paradigm, had the target object appeared in a location different from that predicted by memory, participants likely would have been slower to perceive the object and more prone to errors since memory was biasing attention away for the actual location of the relevant stimulus. Thus, while having an interactive architecture in which memory can predict future outcomes and adaptively bias attention is often beneficial, this dynamic interplay between memory and attention can also lead us astray when the environment is in flux. Under such conditions, it may be more advantageous for attention to be guided by salient perceptual events rather than by memory. Future research could shed light on whether memory-guided attentional orienting occurs relatively automatically once knowledge has been well encoded in memory, as well as how such emerging knowledge, when in error and in conflict with peripheral visual cues, can be overridden.

Of course, not only can memory sometimes bias attention in counterproductive ways, but the way in which attention is oriented during learning can sometimes carry steep costs for memory. In particular, when we focus our attention on one particular feature of a stimulus or experience, we are, by nature, ignoring or perhaps even suppressing the representations of other dimensions. Thus, while Turk-Browne et al. (2006) reveal the simultaneous benefits of attention for implicit and explicit encoding, other recent fMRI data demonstrate that attentional selection against a stimulus can decrease neural activity in stimulus-selective visual association cortices, while also reducing behavioral priming and explicit memory (Yi and Chun, 2005; Gazzaley et al., 2005). At present, it is unclear whether these potentially negative consequences of attention propagate along the MTL circuit, possibly exerting their mnemonic costs by altering hippocampal encoding responses.

Taken together, the findings of Turk-Browne et al. (2006) and Summerfield et al. (2006) illustrate that attention and memory work in concert, with attention influencing which memories are formed and memory guiding how visuospatial attention is allocated (thus, influencing perception). These important observations enhance our understanding of the interplay between attention and memory, revealing the power of attention for determining what aspects of our daily experiences are stored in implicit and explicit memory, as well as how such memories, once encoded, can shape subsequent perception through wresting control of attention.

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Navigating the Anterior-Posterior Axis with Wnts

Recent studies have begun to shed light on the molecular guidance cues controlling anterior-posterior axon guidance. Two recent studies in the current issue of *Developmental Cell* show that Wnts play critical roles in patterning processes and directing neuronal migration in *C. elegans*. Together with previous findings in vertebrates and flies, these new results establish conserved function of Wnts in A-P guidance.

Despite their enormous numbers and complexity, axonal networks are extremely carefully organized. Much of the scaffold of the network is established during earlier developmental stages, when growth cones navigate in embryonic structures. Remarkably, early growth cone navigation largely follows the logic of embryonic patterning along the same major body axes: anterior-posterior (A-P) and dorsal-ventral.

Axon guidance cues along the dorsal-ventral axis are relatively well understood. For example, Netrins and Slits are conserved cues that play roles in directing growth cones along the dorsal-ventral axis as they grow toward or away from the midline (Dickson, 2002). Little has been known about the identity of the cues axons recognize along the A-P axis. This gap in understanding has begun to be filled with the realization that Wnt family proteins act as directional guidance cues in the A-P axis of the vertebrate spinal cord (Lyuksyutova et al., 2003; Imondi and Thomas, 2003; Liu et al., 2005; Dickson, 2005). Ascending sensory axons are attracted to higher concentration of Wnts anteriorly via Frizzled 3, a seven transmembrane domain receptor, and conversely, descending corticospinal tract axons are repelled from higher levels of Wnts via Ryk (Derailed), a Wnt receptor first found to mediate Wnt repulsion in *Drosophila*. A guidance role for Wnts is conserved in the *Drosophila* ventral nerve cord, where Wnt5 determines the pathway choice during midline crossing, allowing a subset of commissural axons to cross the midline only through the anterior commissure in each segment because they avoid Wnt5 in the posterior commissure via the Derailed receptor (Yoshikawa et al., 2003). Whether Wnts have a global A-P guidance role in *Drosophila* in addition to this intrasegmental A-P role is unknown.

In the current issue of *Developmental Cell*, two elegant papers provide compelling evidence that multiple Wnts act as directional cues to control the A-P migration of growth cones and neuronal cell bodies as well as the initial polarity of neuronal processes in *C. elegans* (Hilliard and Bargmann, 2006; Pan et al., 2006). A third independent study also led to the finding that Wnt signaling controls neuronal polarity in the A-P axis in *C. elegans* (Prasad and Clark, 2006). These new exciting findings not only establish a conserved role of Wnt family signaling proteins in axon patterning along the long axis in animals but also provide intriguing new insights into the diverse mechanisms neurons adopt to utilize the directional information provided by Wnts. Given the number of Wnt proteins and receptors and their multitude of mechanisms, this family of guidance cues may play a major role in circuit assembly along the A-P axis.

Wnt Signaling in A-P Guidance in *C. elegans*

The search for A-P guidance mechanisms in *C. elegans* was first conducted by investigating neuronal cell migration along the A-P axis. Cynthia Kenyon's laboratory identified *wnt/egl-20* as a gene required for normal A-P migration of the QL and QR neuroblasts, which give rise to sensory neurons on the left and right sides of the worm. *frizzled/lin-17* and *frizzled/mig-1* were also shown to be part of this regulatory system (Harris et al., 1996). Subsequent analyses established that QL and QR cells respond differently to EGL-20 in a dose-dependent manner, such that QL is more sensitive to EGL-20 than QR. High levels of EGL-20 promote posterior migration by activating the canonical Wnt gene expression pathway in QL, inducing expression of the Hox gene *mab-5* and a change in cell identity and A-P position (Maloof et al., 1999). Low levels of EGL-20 promote anterior migration of QR through a different and unknown pathway (Whangbo and Kenyon, 1999). Because the QR descendents do not require a localized source of EGL-20 to migrate anteriorly, EGL-20 was thought to be a permissive cue rather than a directional guidance cue for A-P cell migration (Whangbo and Kenyon, 1999).

Taking advantage of the wealth of mutant *wnt* and *frizzled* strains available in *C. elegans*, Gian Garriga's group from the University of California, Berkeley systematically analyzed the function of Wnts and Frizzled receptors in neuronal migration and axon guidance along the A-P axis in *C. elegans*. Remarkably, they found that all five Wnts and four Frizzleds in *C. elegans* function in neuronal migration and a subset of Wnts control anterior axon guidance, and at least Wnt/EGL-20 can function as a repellent that is sensed by Frizzled proteins. The hermaphrodite-specific neurons (HSNs), a pair of motor neurons that control egg laying, are born at the posterior end of the worm body and migrate anteriorly. Wnt/EGL-20 and Frizzled/MIG-1 are required for this anterior migration: mutations in either gene cause HSNs to terminate their migration posterior to their normal positions. Although single mutants of four other *wnt* genes, *cwn-1*, *cwn-2*, *lin-44*, and *mom-2*, showed few or no