systems. What is clear is that the work of Zhang *et al.* [5] makes a unique contribution to addressing the important question of mechanical integration during morphogenesis.

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Department of Zoology, University of Wisconsin, 1117 W. Johnson St., Madison, WI 53706, USA.
E-mail: jdhardin@wisc.edu

DOI: 10.1016/j.cub.2011.03.052

Animal Cognition: Monkeys Recall Previously Seen Images

A recent study has found that rhesus macaques can recall newly presented shapes: this demonstration of recall in non-human primates suggests that some animals have recollection processes similar to those of humans.

Bennett L. Schwartz

Consider, as a few novelists have done, that the only witness to a serious crime is a non-human primate [1,2]. Can a rhesus monkey or other primate bring an image to mind of the criminal? And how might that monkey relay that information to investigators? Implicit in these questions is the question of whether or not, like humans, animals can have recollective experiences [3]. Recollective experience refers to the notion that we maintain conscious images, thoughts, or feelings that refer to past events [4]. Much research with humans has shown that, in order to demonstrate recollective experience, a person must be able to recall the past event, not simply recognize it [5,6]. Until now, however, no research has even been able to demonstrate recall, and therefore conscious recollective experience, in a non-human animal. Basile and Hampton [7] have addressed precisely this question in a study reported in this issue of *Current Biology*.

In humans, recall tests are easy to conduct, because all you need to do is ask, and we can respond verbally. In some cases, when a visual memory is required, some people can make accurate drawings from memory. As Basile and Hampton [7] point out, however, animals can neither talk nor draw; consequently, all past research looking at animal memory has involved recognition tests, in which the animal must match their memory with a physically present signal. In match-to-sample tasks, for example, animals must choose an image or sound that they were exposed to earlier [8,9]. That is, in the visual domain, the animals must choose between an image that was presented earlier and a novel image. Similarly, in the auditory domain, an animal must choose between two sounds presented sequentially (or simultaneously), one of which was presented earlier [10]. Note that, in a delayed match-to-sample task, the to-be-remembered stimulus is presented to the animal at the time of test, and the animal must choose to accept it or reject it. In their new work, however, Basile and Hampton [7] used touch screen technology to demonstrate that monkeys, like humans, can remember images that are absent at the time of test.

Consider an experiment in primate memory conducted by Hoffman and colleagues [11]. In a delayed match-to-sample test, rhesus macaques saw a picture presented for three seconds; after a delay of either one second or 10 seconds, the monkey saw the same image and a new image not seen before. The monkeys had to touch the image

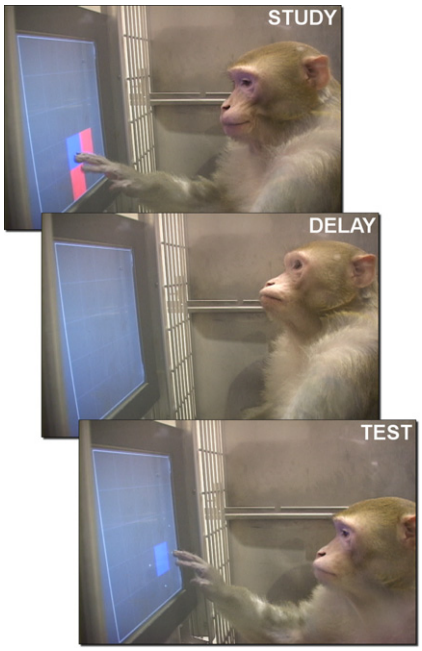

Figure 1. A rhesus monkey engaged in the memory recall task.

The top photograph shows the rhesus monkey being presented with the to-be-remembered stimulus. The monkey touches the blue square to indicate that it has seen the stimulus. The second photograph depicts the retention interval, that is, the time between the presentation of the to-be-remembered stimulus and the time when the monkey is asked to recall the information. The third photograph shows the monkey beginning to recall the stimulus. Important in this study is that the red squares are not present to be recognized. Instead the monkey must "draw" them on the touch screen by touching their relative positions to the retrieval cue (the blue square). (Photograph courtesy of Ben Basile; reprinted with permission).

that corresponds with what they saw earlier in order to receive a food reward. Note that, translated into the language of human memory, this test is a recognition test. The monkey must match what is in memory with one of the two presented stimuli. A vague sense of familiarity can guide this response in addition to an experience of remembering the earlier presentation. Many variations on this delayed match-to-sample have been used [12].

In contrast, Basile and Hampton [7] required five rhesus macaques (*Macaca mulatta*) to reproduce from memory simple figures on a touch screen, thereby simulating a proper recall test (Figure 1). During the study phase, the monkeys saw a shape consisting of two or three boxes. Then, the shapes disappeared. Following a retention interval of one second up to 128 seconds, the monkeys then saw one of the two or three boxes presented at a new location on the touch screen. The monkeys were then required to touch the screen in the location where the absent boxes had been relative to the presented box during the earlier presentation. Touching each box 'drew' that part of the shape they had seen earlier (Figure 1). Success on this task earned the monkeys food rewards. Unlike the delayed match-to-sample task, however, the to-be-remembered stimulus was not physically present at the time of test.

This was a challenging task for the monkeys. In initial training, their performance was relatively poor (28%), but significantly better than chance (12.5%), given that there were eight potential locations that they could touch. Later, their performance rose to a much higher level (80%). Basile and Hampton [7] argue that the monkeys could not have solved this task using familiarity alone, as the to-be-remembered boxes were not present. Familiarity processes can permit recognition but are less likely to be implicated in recall [3,4]. A process analogous to recollection, however, would allow the monkeys to succeed at the task. Thus, their above-chance accuracy suggests a process similar to that of recollection in humans. When the monkeys were given a recognition test, in which the figures were present, their performance improved, as now they could rely on familiarity as well as recollection. Moreover, when the monkeys were given a novel transfer task in which they were required to reproduce three block shapes, they did so immediately at above-chance rates, just as would happen with humans using recollective processes.

Does their procedure really model recall in a non-verbal species? It could be argued that the monkey has only to point to one of eight locations centered around the square that is used as the cue for recall. In this sense, it is like a recognition test. Unlike all other tests with non-human primates, however, the to-be-remembered stimulus, or a symbol for that stimulus, is not actually present. This is generally considered the important difference between recognition and recall in human memory. Therefore, this new paradigm does tap the ability of rhesus monkeys to recall information. It could also be argued that the short retention intervals only allow for an assessment of working memory. But Basile and Hampton [7] make no claims that their results shed light on differences in recall from working memory and in recall from long-term memory. Their experiment is designed to demonstrate the ability of the monkeys to do recall tests and does not look at differences among memory systems.

The ability to recall the past is important for an organism, as it frees the organism from being locked into what is here, what is now, what it can see and hear at the moment. Evolutionary speculation on the adaptive advantage of recollective experience centers on the observation that recollective experience can be used to model the future [3]. Organisms that can remember the past may be able to plan for the future. Recent findings that point to the ability of chimpanzees to plan for the future [13] suggest that they, perhaps like the rhesus monkeys studied by Basile and Hampton [7], may not be locked into the present. Animals that cannot recall may be stuck in the present; however, the current data suggest that monkeys, like humans, do recall and perhaps have recollective experiences.

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Department of Psychology, Florida International University, University Park, Miami, FL 33199, USA.
E-mail: bennett.schwartz@fiu.edu

DOI: 10.1016/j.cub.2011.03.040

Circadian Biology: The Supporting Cast Takes On a Starring Role

Brain circuits are generally thought to consist solely of neurons communicating with other neurons. In *Drosophila*, glia-to-neuron signaling has now been shown to be critical to the function of the circadian circuit.

Leslie C. Griffith

Glia have been regarded by many as the nervous system equivalent of extras in a movie crowd scene: they are required to set the mood but do not drive the plot. Well-documented roles for glia in vertebrates are numerous. They include metabolic and trophic support, developmental pathfinding, scavenging of neurotransmitters and cell debris, electrical insulation of axons, as well as the chemical isolation of cellular compartments. Glia have not, however, had much of a chance at the spotlight in terms of behavior. In *Drosophila*, glia have also been shown to carry out critical support functions, but the genetic tools available have now allowed researchers to begin to examine their roles in directly shaping nervous system output. In a recent issue of *Current Biology,* Ng and coworkers [1] demonstrate that calcium-dependent glia-to-neuron signaling regulates the circadian locomotor rhythm.

The idea that glia have a role in circadian rhythms has been around since the identification of the molecular clock in *Drosophila*. The cloning of the first circadian gene, *period,* allowed researchers to establish a foothold in the cellular clock. Looking for cells that expressed PERIOD in a cyclic manner, they hoped to identify a neural circuit for timekeeping. Surprisingly, the cells they found included a substantial number of glia [2,3]. This cyclic expression of clock genes in glia is not just an oddity of flies. PERIOD cycling has also been seen in astrocytes of the mammalian suprachiasmatic nucleus [4], suggesting that glia may be a component of all animal clocks. Consistent with this, mosaic studies in flies found that expression of PERIOD in ventral brain glia, without any neuronal expression, was actually sufficient to support weak rhythms [5]. For many years, however, the role of glia in rhythms remained relatively unexplored.

Glia resurfaced in the clock when Suh and Jackson [6] showed that the circadian function of the *ebony* gene, which regulates locomotor output downstream of the clock, resided in glia. EBONY is an N-β-alanyl-biogenic amine synthetase; it attaches β-alanine to a variety of neurotransmitter substrates. The proximity of *ebony*-expressing glia to dopaminergic neurons, and the known function of dopamine in arousal and locomotor activity, led the authors to speculate that N-β-alanyl-dopamine (NBAD) might regulate dopaminergic function as a gliotransmitter. Direct signaling to neurons from glia had not been previously shown in *Drosophila.*

Ng and colleagues [1] tested this idea that active, calcium-dependent signaling processes are required in astrocytic glia to drive circadian locomotor behavior. Using genetic tools available in *Drosophila* to spatially and temporally limit transgene expression, the authors showed that glial disruption of membrane potential by expression of a constitutively open sodium channel, misregulation of glial calcium by RNA interference (RNAi) knockdown of sarco/endoplasmic reticulum Ca^{2+}-ATPase and blockade of vesicle trafficking by a dominant negative dynamin each can cause arrhythmicity in constant conditions (dark:dark, DD) after circadian entrainment in a normal light:dark cycle. The manipulations used were reversible and designed to limit molecular disruptions to defined times in adulthood. This is particularly important since the ability of animals to regain normal rhythms following a period of signal disruption demonstrated that there was no permanent damage to glia or the locomotor system.

Interestingly, the phase of the rhythm after restoration of normal cellular function in DD was the same as that of the pre-disruption rhythm. This implied that the central clock was still 'ticking' even though the animals were behaviorally arrhythmic. Consistent with this, circadian cycling of the abundance and localization of PERIOD and PDP1ε proteins in lateral clock neurons was normal on day 2 of DD while signaling was disrupted. This makes a strong case that the process that was being affected by these glial manipulations was one that was critical to the output of the circadian clock, not to the functioning of the central clock itself.

Given that alterations in glial activity did not affect molecular clock function in the canonical neuronal clock circuit, an obvious question to ask was whether cycling of clock proteins in the glia themselves was at the heart of their role in locomotor rhythmicity. To address this, the authors used glial-specific RNAi transgenes to knock down levels of PERIOD and another circadian protein, CRYPTOCHROME. Neither manipulation affected motor rhythms, indicating that having an oscillating molecular clock within glia is not necessary for locomotor rhythms.

While the transcriptional machinery that makes up the molecular clock appeared to be normal in clock neurons, one of the peptide transmitters of the ventral lateral neurons (LNvs) was significantly altered in abundance when glia were