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LEARNING AND MEMORY

Day to remember

Learning and memory are known to be influenced by the time of day, but the nature and mechanism of this modulation has been elusive. Now, a new study shows that melatonin, a hormone released in a circadian fashion, affects memory consolidation in zebrafish.

Cahill and colleagues assessed memory formation in diurnal zebrafish using an active-avoidance conditioning paradigm, in which the zebrafish learned to associate a particular compartment of their tank with mild electric shocks. They found that zebrafish that were conditioned during the day learned more quickly than those that were conditioned at night and had significantly better retention when tested 24 hours after conditioning. Furthermore, when the zebrafish were kept in constant darkness for several days, those that were conditioned during the period of their circadian cycle that corresponded to daytime (their subjective daytime; SD) outperformed those that were conditioned during their subjective night (SN). This implicated the endogenous circadian system in the effect of time-of-day on learning.

To ascertain whether the modulation of learning ability was due to altered memory formation or memory retrieval, the authors again used zebrafish that had been kept in constant darkness for several days. They found that those that were conditioned during their SD and then tested during their SN 36 hours later had significantly higher memory retention than those that were conditioned during their SN and tested during their SD. Thus, the circadian system was affecting memory formation rather than retrieval.

Melatonin release peaks during the night and falls during the day, and melatonin has been shown to affect neuronal firing in the hippocampus. The authors therefore decided to investigate whether melatonin mediates the effects of the circadian system on memory formation. They found that bathing the zebrafish in 50 μM melatonin prior to SD conditioning significantly suppressed memory formation, whereas administration after conditioning or prior to testing had no effect. Furthermore, administration of a melatonin-receptor antagonist prior to SN conditioning significantly improved memory retention, as did removal of the pineal gland, the site of melatonin release.

Taken together, these results show that memory formation in zebrafish is inhibited during the night relative to the day, and that this modulation is mediated at least in part by circadian melatonin release. This might direct future research into improving mental performance in humans.

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ORIGINAL RESEARCH PAPER Rawashdeh, O., Hernandez de Borsetti, N., Roman, G., & Cahill, G. M. Melatonin suppresses nighttime memory formation in zebrafish. *Science* **318**, 1144–1146 (2007)