How the brain focuses on what's in mind

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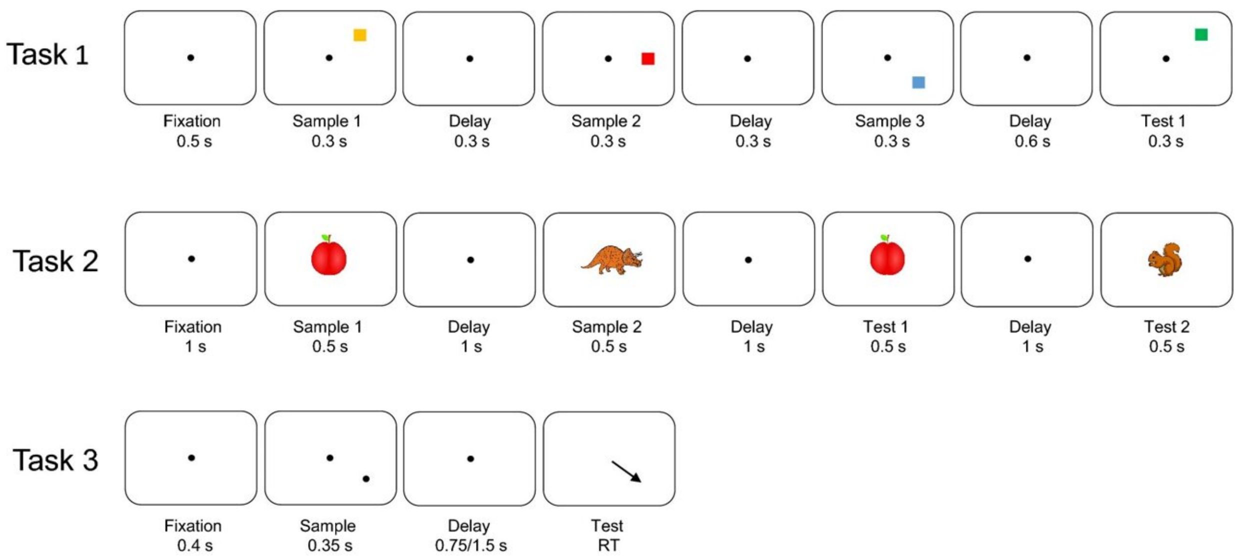

Task structure of the 3 working memory tasks. Top: Structure of Task 1. The monkeys were presented with a sequence of 3 colored squares in 3 distinct positions. After a brief delay, the monkeys were exposed to a new sequence of up to 3 squares. They reported with a saccade to the first square that had changed color between sample and test sequences (one of the squares always changed, in the above case the first). Middle: Structure of Task 2. The monkeys were presented with a sequence of 2 objects foveally. After a brief delay, the monkeys were exposed to a new sequence of 2 objects. They reported by lifting a bar if the test sequence did not match the sample sequence. Bottom: Structure of Task 3. Delayed saccade task with 2 possible delay lengths. On 6/7 trials, there was a 0.75 s delay, on the rest there was a 1.5 s delay. Credit: *Scientific Reports* (2022). DOI: 10.1038/s41598-022-18577-y

Working memory, that handy ability to consciously hold and manipulate new information in mind, takes work. In particular, participating neurons in the prefrontal cortex have to work together in synchrony to focus our thoughts, whether we're remembering a set of directions or tonight's menu specials. A new study by researchers based at The Picower Institute for Learning and Memory at MIT shows how that focus emerges.

The key measure in the study in *Scientific Reports* is the variability of the neurons' activity. Scientists widely agree that less variability activity means more focused attunement to the task. Measures of that variability have indeed shown that it decreases when humans and animals focus during working memory games in the lab.

In several studies between 2016 and 2018 lead author Mikael Lundqvist and co-senior author Earl K. Miller showed through direct measurements of hundreds of neurons and rigorous modeling that bursts of gamma frequency rhythms in the prefrontal cortex coordinate neural representation of the information held in mind. The information representation can be measured in the synchronized spiking of populations of individual neurons. Bursts of beta frequency rhythms, meanwhile, implement the brain's manipulation of that information. The theory, which Miller dubbed "Working Memory 2.0" challenged a long-held orthodoxy that neurons maintain working memory information through steady, persistent activity. Proponents of that older model, which emerged from averaged measurements made in relatively few neurons, used computer-based modeling of brain activity to argue that reduced variability cannot emerge from intermittent bursts of rhythmic activity.

But the new study shows that the reduced variability, does, in fact, emerge.

"We used actual neural activity recorded from the prefrontal cortex to show that the rhythmic bursts reduce their variability as animals focus on a task," said Miller, Picower Professor in MIT's Department of Brain and Cognitive Sciences.

"All the phenomena we think that is important working memory, the bursts of spiking the bursts of gamma are doing what they should do," Miller said. "It's all becoming more focused when the animals are performing a working memory task and that naturally reduces the variability. It shows how these new rhythmic elements of working memory are totally compatible with your brain focusing its activity on the task at hand."

Direct observations

In the study, Lundqvist and the team measured gamma bursts and individual neural spiking among hundreds of neurons as six animals played three different working memory games. They also analyzed how much that activity varied from trial to trial, using a calculation called a "Fano factor."

As the animals proceeded through each task, gamma bursts and spiking rates showed clear differences from the baseline period, consistent with them being modulated by demands of the task. For instance, in one task they would transiently peak as each item to be remembered was presented, and then again when the animals' memory was to be tested.

While activity was clearly modulated by the task, so was the variability from trial to trial. In each task, they found that variability was highest before the tasks began—a "baseline" condition in which the animals could think about whatever they wanted. But once the animals had to focus on the task again, their gamma bursts and neural spiking became much more similar to what it had been the last time or the next time they did the task. Moreover, the decreases in variability also tracked tightly with key moments of the task (e.g. presentation of something to remember).

"Our findings suggest that there are population burst events dictated by various cognitive threads all the time," said Lundqvist, a former postdoc in Miller's lab who is now a principal researcher at the Karolinska Institutet in Stockholm. "As we focus on a specific task, population events related to other cognitive threads quiet down. As a result, single neuron spiking becomes more dictated by that particular task."

The reduction of variability was not only true in time, but also in space. Areas of the prefrontal cortex where gamma bursts and spiking represented task information showed much greater decreases in variability than areas that were not representing task information.

Simulation suggests causation

While the direct measurements showed reductions in variability commensurate with task demands for focused thinking, the team also investigated whether the reductions in spike variability were the result of reductions in the gamma bursting variability.

Using their measurements of gamma bursts and their variability, they played with simulating variations in spiking (for instance the rate of spiking), to see if reductions in gamma burst variation necessarily led to reductions in spiking variation.

"We used a simple model where we gave neurons two distinct firing rates depending on if there was a currently an ongoing gamma burst event or not," Lundqvist said. "Then simply based on the timing of recorded gamma burst events we made thousands of spike trains. These artificial spike trains had very similar changes in variability as those originally recorded. This suggests that the participation in population events largely drive this reduction."

In all, the scientists said, they found that variability decreases with working memory task demands and that is guided by the timing and placement of bursts of gamma rhythms.

"We found that the task-related modulation of bursts of spiking and gamma power during a working memory task resulted in the cross-trial reduction in the variability of neural activity," the authors wrote. "Further we found that a direct relationship between the reduction of the variability of gamma bursting and the reduction of spiking variability. They co-occurred both in time and space."

More information: Mikael Lundqvist et al, Reduced variability of bursting activity during working memory, *Scientific Reports* (2022). DOI: 10.1038/s41598-022-18577-y

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