Ready, set…GO! Scientists discover a brain circuit that triggers the execution of planned movement

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While waiting at a red light, the brain has planned the precise movements needed to make a smooth turn. However, these plans turn into action only when the light turns green. Scientists from the Max Planck Florida Institute for Neuroscience, HHMI's Janelia Research Campus, the Allen Institute for Brain Science, and others have now discovered a brain circuit critical for triggering movement in response to environmental cues. Credit: Julia Kuhl

Planned movement is essential to our daily lives, and it often requires delayed execution. As children, we stood crouched and ready but waited for the shout of "GO!" before sprinting from the starting line. As adults, we wait until the traffic light turns green before making a turn. In both situations, the brain has planned our precise movements but suppresses their execution until a specific cue (e.g., the shout of "GO!" or the green light). Now, scientists have discovered the brain network that turns plans into action in response to this cue.

The discovery, published in the scientific journal *Cell*, results from a collaboration of scientists at the Max Planck Florida Institute for Neuroscience, HHMI's Janelia Research Campus, the Allen Institute for Brain Science, and others. Led by co-first authors Dr. Hidehiko Inagaki and Dr. Susu Chen and senior author Dr. Karel Svoboda, the scientists set out to understand how cues in our environment can trigger planned movement.

"The brain is like an orchestra," said Dr. Inagaki. "In a symphony, instruments play diverse tunes with different tempos and timbres. The collective of these sounds shapes a musical phrase. Similarly, neurons in the brain are active with diverse patterns and timing. The ensemble of neuronal activities mediates specific aspects of our behavior."

For example, the motor cortex is a brain area that controls movement.

Activity patterns in the motor cortex are dramatically different between the planning and execution phases of movement. The transition between these patterns is critical to trigger movement. Yet, the brain areas controlling this transition were unknown. "There must be brain areas acting as the conductor," said Dr. Inagaki. "Such areas monitor environmental cues and orchestrate neuronal activities from one pattern to the other. The conductor ensures that plans are converted into action at the right time."

To identify the neural circuit that serves as the conductor to initiate planned movement, the team simultaneously recorded the activity of hundreds of neurons while a mouse performed a cue-triggered movement task. In this task, mice were trained to lick to the right if whiskers were touched or to the left if whiskers were not touched. If the animals licked in the correct direction, they received a reward. However, there was a catch. The animals had to delay their movement until a tone, or "go cue," was played. Only correct movements after the go cue would be rewarded. Therefore, mice maintain a plan of the direction they will lick until the go cue and execute the planned lick after.

The scientists then correlated complex neuronal activity patterns to relevant stages of the behavioral task. The researchers found brain activity occurring immediately after the go cue and during the switch between motor planning and execution. This brain activity arose from a circuit of neurons in the midbrain, thalamus, and cortex.

To test whether this circuit acted as a conductor, the team used optogenetics. This approach enabled the scientists to activate or inactivate this circuit using light. Activating this circuit during the planning phase of the behavioral task switched the mouse's brain activity from motor planning to execution and caused the mouse to lick. On the other hand, turning off the circuit while playing the go cue suppressed the cued movement. The mice remained in a motor planning stage as if they had not received the go cue.

This work by Dr. Inagaki and his colleagues identified a neural circuit critical for triggering movement in response to environmental cues. Dr. Inagaki explains how their findings demonstrate generalizable features of behavioral control. "We have found a circuit that can change the activity of the motor cortex from motor planning to execution at the appropriate time. This gives us insight into how the brain orchestrates neuronal activity to produce complex behavior. Future work will focus on understanding how this circuit and others reorganize neuronal activity across many brain regions."

In addition to these fundamental advances in understanding how the brain functions, this work has important clinical implications. In motor disorders, such as Parkinson's disease, patients experience difficulty in self-initiated movement, including difficulty in walking. However, adding environmental cues to trigger movements, such as lines on the floor or auditory tones, can dramatically improve a patient's mobility. This phenomenon, known as paradoxical kinesia, suggests that different mechanisms in the brain are recruited for self-initiated movement and cue-triggered movement. Discovering the brain networks involved in cue-triggered movements, which are relatively spared in Parkinson's disease, may help to optimize treatment.

More information: Hidehiko K. Inagaki et al, A midbrain-thalamus-cortex circuit reorganizes cortical dynamics to initiate movement, *Cell* (2022). DOI: 10.1016/j.cell.2022.02.006

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