Clarifying prefrontal neurons' roles in flexible behavior

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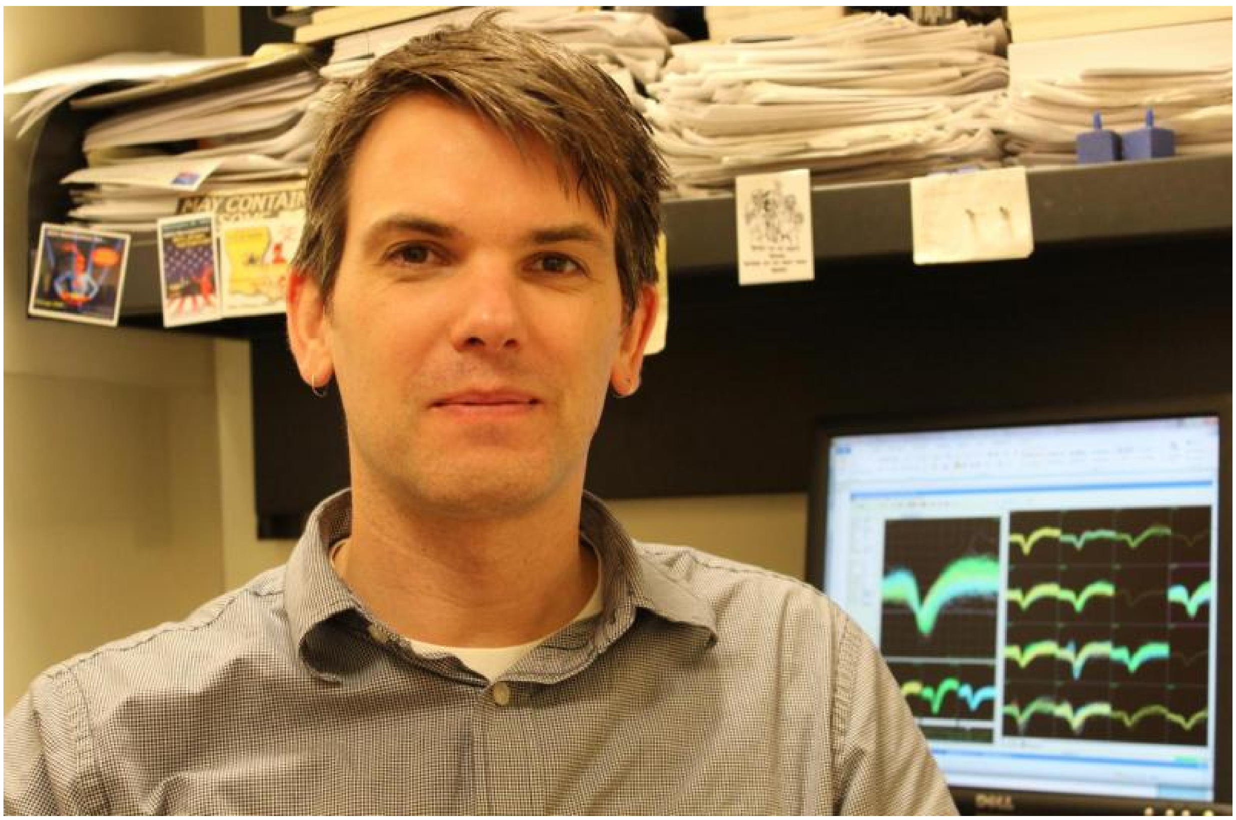

Results of a new study reported this week suggest that adjusting behavior based on previous events involves an unexpected mix of neurons working together in the brain's prefrontal cortex. Credit: UMass Amherst

Results of a new study reported this week by David Moorman of the University of Massachusetts Amherst and Gary Aston-Jones of Rutgers

University suggest that adjusting behavior based on previous events involves an unexpected mix of neurons working together in the brain's prefrontal cortex.

Findings appear in this week's early online version of *Proceedings of the National Academy of Sciences*.

As Moorman explains, "One prominent hypothesis, based on previous research, argues that neurons in the dorsal prefrontal cortex control active behaviors related to 'going' and that different neurons in ventral prefrontal regions control inhibitory behaviors related to 'stopping.' We tested this hypothesis by recording the activity of neurons in both of these prefrontal regions in rats while they pressed levers to get rewards."

Instead of finding that one area controlled going and the other stopping, he adds, "we found that both regions worked together to provide information about the relationship between actions and outcomes, essentially informing the animal what would happen if it pressed or did not press a lever, in our experiment. The neurons basically signaled whether or not the animal understood the 'rules of the game,' which is important for all animals, including people. It lets them know when to exert effort to get a reward and when to conserve energy when nothing is available."

The authors say this new understanding in rats may in the future help to inform research on how these brain systems may be disrupted in human psychiatric disorders such as schizophrenia or addiction, both characterized by an impaired ability to adjust one's actions based on events.

"Understanding which circuits encode this contextual information, and how, allows us to pinpoint targets for treatment of complicated psychiatric diseases," Moorman adds. He did this work while at the

Medical University of South Carolina; he is now an assistant professor in the department of psychological and brain sciences at UMass Amherst.

These experiments involved making a sweetened drink available to rats who learned they could get the reward by pressing a lever. The researchers then extinguished this behavior by withholding the sweet reward even when the animal pressed the lever. Tiny electrode probes thinner than a human hair were implanted painlessly in both dorsal and ventral prefrontal cortex to measure neuronal activity.

"We went into this expecting to see 'go' neurons activate with 'go' behaviors and 'stop' neurons with extinction," Moorman says. "What we found instead is that neurons would fire in both areas, and would keep firing in both areas during extinction." In fact, both 'go' and 'stop' neurons fired more frequently, or strongly, when the animal expected a reward and went for it, as well as when the animal did not expect a reward and held back. A subtle, but important difference than what they expected, Moorman says.

"It was surprising and interesting," he notes. "This is the first time we have tested the dorsal vs. ventral hypothesis in this way. What we observed adds a new spin; the neurons in both places are working together to make these behaviors happen. Clearly they don't fall into black and white, dichotomous functions. They work together to control behavior," he notes.

"We concluded that as the animal learns what the outcome is going to be, this prefrontal neuronal firing is a marker of learning the rules," the neuroscientist says.

"It turns out that there is other research that lines up perfectly with this. We found support for the idea that context and rules matter, and one of the prefrontal cortex's jobs is to make sense of all information. When the neurons fire, it reflects that the rat is able to correctly recognize the relationship between actions and outcomes. This is a new way of thinking about how these two different brain areas contribute to these processes."

Moorman feels that neuroscience is migrating away from simpler to more sophisticated ideas of what these brain areas are doing. "This paper emphasizes that the prefrontal cortex, and the brain as a whole, is a complicated system involved in complicated behavior. We still have a lot to figure out and we need to embrace this complexity to understand how everything works," he notes.

In the future the researchers plan to explore this line of research further to "really understand how neuron activity in the prefrontal cortex encodes behavior, and to what degree these signals vary or are consistent. For example, are there specific circuits that fire together to control these behaviors? And how are these circuits disrupted in mental illness? I'm looking forward to the answers leading us on to more questions."

More information: Prefrontal neurons encode context-based response execution and inhibition in reward seeking and extinction, DOI: 10.1073/pnas.1507611112

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