Activation of brain region can change a monkey's choice

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Barbary macaques. Credit: Wikipedia/Flickr/Karyn Sig

Artificially stimulating a brain region believed to play a key role in learning, reward and motivation induced monkeys to change which of two images they choose to look at. In experiments reported online in the journal *Current Biology*, researchers from Massachusetts General

Hospital (MGH) and the University of Leuven in Belgium confirm for the first time that stimulation of the ventral tegmental area (VTA) – a group of neurons at the base of the midbrain – can change behavior through activation of the brain's reward system.

"Previous studies had correlated increased activity in the primate VTA with positive events experienced by the animal but could not prove that VTA activity actually caused behavioral changes," says Wim Vanduffel, PhD, of the Martinos Center for Biomedical Imaging at MGH, corresponding author of the *Current Biology* paper. "Studies in rodents have shown that artificially manipulating VTA activity strongly influences behavior, and our work has bridged the gap between rodent and primate." Vanduffel is also head of the Laboratory for Neuro- and Psychophysiology at the University of Leuven.

To investigate the direct impact of VTA activation on primate behavior, the research team used high-resolution magnetic resonance imaging to guide the placement of microelectrodes within the VTAs of macaque monkeys. In the initial set of experiments, the animals were presented with a pair of images – for example a star and a ball – and could freely chose to look at one image or the other, with their choice measured by their eye movement. Each animal was trained by means of a juice reward to look first at a white square at the center of the visual field and then at either of the paired images.

After establishing each animal's preference, based on which image was looked at most frequently, mild stimulation was applied to the VTA when the animal happened to look at the initially nonpreferred image. Soon the animal's preference changed, and it most frequently looked at what previously had been the less favored image. When the VTA stimulation was then applied to the initially preferred image, the monkeys soon changed their preference back to the original choice.

In a second set of experiments, after the initial image preference was established, an animal watched a 20-minute video, during which the two images were randomly presented every 5 seconds. Whenever the initially nonpreferred image was presented, it was accompanied by mild VTA stimulation. Subsequent repetition of the preference test showed that the animal's choice had shifted to the image reinforced by VTA stimulation.

Functional MR imaging taken while the animals received either a juice reward or VTA stimulation revealed that both induced activation of brain regions that previous studies in humans and other primates have associated with reward signaling by means of the neurotransmitter dopamine. The level of VTA stimulation required to activate these structures was considerably less than the amount required to reinforce or change behavior in the earlier experiments.

"Our study showed that the timing of VTA stimulation is important – when stimulation happens immediately after an action is performed, the monkey is more likely to perform that action – and that it applies 'value' to a particular stimulus and motivates future behavior," says Vanduffel, who is an assistant professor of Radiology at Harvard Medical School. "Other studies have implicated the VTA in learning based on negative, as well as positive reinforcement, and a recent rodent study found that increasing VTA activation can relieve depression, possibly by increasing motivated behavior. Our findings lay the groundwork for further investigation of the role of the VTA in reinforcing and regulating motivated behavior."

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