Researchers find discrepancies in brain reactions due to acute versus permanent neural manipulations

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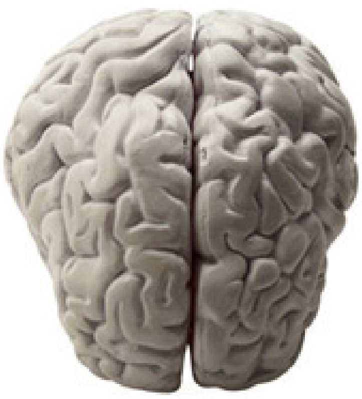

(Medical Xpress)—A team of researchers with Harvard University and the Simons Foundation has found that using techniques to acutely disable brain parts of rats and zebra finches can lead to different behavioral results than techniques that involve causing lesions. In their paper published in the journal *Nature*, the researchers describe how they tested both approaches on rats and birds and the differences they found between the techniques. Thomas Südhof with Stanford University offers a News & Views piece on the work done by the team and suggests ways for future researchers to proceed in light of the new findings.

For many years, the tried and true approach to figuring out which parts of the brain were responsible for controlling what abilities, was to simply cut open the brain of an animal and disable one small portion (a process known as lesioning) and then look for changes in behavior. In more modern times, researchers have discovered that it is possible to cause parts of the brain to stop working temporarily using drugs injected into certain areas instead, causing what is known as acute effects. Even more recently, researchers have found that neuronal activity can be manipulated using optogenetic activation techniques. The assumption has been that disabling portions of the brain using lesioning would cause the same changes in behavior as injecting drugs or using lasers. But now, this research suggests that is not the case at all.

The researchers found that disabling a portion of the brain in rats that was known to store information about remembering an activity that had been learned, using acute techniques resulted in the rats forgetting how to do the task—but lesioning the area did not. They found roughly the same thing when using acute techniques to stifle the ability to sing in zebra finches—lesioning the same areas did not interfere with their ability to sing. In both experiments, the researchers noted that lesioning did cause the same impact in both animals for a very short time, but then the impact went away on its own, suggesting a neural network impact.

These findings are likely to have a profound impact on the science of neurobiology going forward—researchers will have to take more factors into consideration when claiming they have figured out what certain parts of the brain (or individual neurons) are responsible for doing. It also suggests that networks of neurons play more of the role in brain controlled abilities than has been thought.

More information: Timothy M. Otchy et al. Acute off-target effects of neural circuit manipulations, *Nature* (2015). DOI: 10.1038/nature16442

Abstract
Rapid and reversible manipulations of neural activity in behaving animals are transforming our understanding of brain function. An important assumption underlying much of this work is that evoked behavioural changes reflect the function of the manipulated circuits. We show that this assumption is problematic because it disregards indirect effects on the independent functions of downstream circuits. Transient inactivations of motor cortex in rats and nucleus interface (Nif) in songbirds severely degraded task-specific movement patterns and courtship songs, respectively, which are learned skills that recover spontaneously after permanent lesions of the same areas. We resolve this discrepancy in songbirds, showing that Nif silencing acutely affects the function of HVC, a downstream song control nucleus. Paralleling song recovery, the off-target effects resolved within days of Nif lesions, a recovery consistent with homeostatic regulation of neural activity in HVC. These results have implications for interpreting transient circuit manipulations and for understanding recovery after brain lesions.