This Week in The Journal

Rats Can Use Neural Prostheses to Follow Infrared Cues

Konstantin Hartmann, Eric E. Thomson, Ivan Zea, Richy Yun, Peter Mullen, et al.

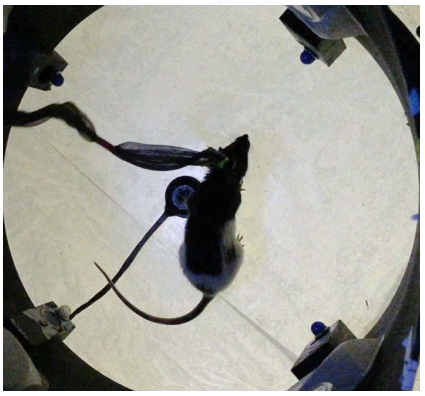
(see pages 2406–2424)

Creating neural prostheses that provide sensory and motor function after injury or degeneration is a major goal in neuroscience. Much progress has been made toward developing robotic arms controlled by neural activity; but this progress has underscored the importance of sensory feedback for precise object manipulation. Researchers are now attempting to develop somatosensory prostheses to interface with motor prostheses. While peripheral prostheses (cochlear implants) have been successful in restoring auditory function, peripheral stimulation may be impractical or ineffective after spinal cord injury or nerve degeneration. Prostheses involving intracortical microstimulation could circumvent these problems.

An important question for the design of intracortical sensory prostheses is how closely electrical stimulation must mimic natural sensory input to be useful. Hartmann, Thomson et al. investigated this question by imparting a new sense—infrared light detection—to rats. Four infrared sensors were mounted around rats' heads and connected to electrodes implanted in the somatosensory barrel cortex (S1). In some rats, sensors were connected to topographically homologous regions of S1: for example, the front-right sensor activated the region normally activated by front-right whiskers. With this setup, rats learned within 4 d to use information from infrared signals to find a reward. In other rats, sensors were connected to topographically non-homologous regions of S1. These rats also learned to perform the task reliably, but they required more sessions to do so.

Most S1 neurons showed greater responses when two inputs were active than when only one was active, and many neurons responded preferentially when both hemispheres were stimulated. Moreover, neurons developed selectivity for specific patterns of stimulation across the four electrodes, and the neuronal population responded most strongly to more commonly occurring stimulus patterns, suggesting responses were altered by experience. Finally, when stimulation patterns that occurred during the task were replayed in naive rats performing an unrelated task, S1 responses to the stimuli were suppressed. This indicates that responses weren't limited to increases in activity and were strongly influenced by behavioral state.

These results demonstrate that adult rat brains can learn to use a new sensory modality and integrate information from multiple inputs to guide behavior. Importantly, although topographical stimulation sped the learning process, it was not essential. This is promising for the development of neural prostheses, because it suggests that precise reproduction of natural stimulus patterns is not necessary for creating functional devices.



Rats learn to use a neural prostheses to follow infrared cues to reward sites. See Hartmann, Thomson et al. for more information and to watch the movie.

Parkin Mutations Alter Membrane Trafficking

Pingping Song, Katarina Trajkovic, Taiji Tsunemi, and Dimitri Krainc

(see pages 2425–2437)

Proper trafficking of membranous vesicles is essential for maintaining neuronal function. Vesicles carry newly synthesized transmembrane and secreted proteins from the endoplasmic reticulum to the Golgi and then the cell surface, where the vesicles fuse with the plasma membrane. Endocytosis allows vesicular proteins and membranes to be recycled, and it regulates expression levels of transmembrane proteins. Endocytic vesicles fuse to form early endosomes, which reorganize to become late endosomes. From there, vesicles carry proteins back to the cell surface, to the Golgi, or to lysosomes for degradation. Vesicles may also form inside endosomes, creating multivesicular bodies that fuse with the cell membrane and release intact vesicles, called exosomes.

Disruption of any of these trafficking pathways can cause neurodegeneration. Indeed, several mutations responsible for inherited forms of Parkinson's disease (PD) occur in proteins that regulate membrane trafficking. One such protein is Parkin, which transfers ubiquitin moieties to other proteins, thus targeting them for lysosomal degradation. In fact, Song et al. report that *parkin* mutations disrupt several endocytic pathways.

Fewer late endosomes were found in skin fibroblasts from patients with *parkin* mutations than in controls, and levels of proteins involved in transport from endosomes to the Golgi were reduced. In contrast, the number of vesicles in multivesicular bodies was increased, as was exosome secretion. These effects were likely mediated partly by reduced Parkin-dependent ubiquitination of Rab7, a small GTPase involved in endosomal trafficking. Although decreases in ubiquitination often result in reduced protein degradation and thus increased protein levels, Rab7 levels were reduced in Parkin-deficient cells, suggesting ubiquitination by Parkin does not target Rab7 for degradation. Instead, loss of ubiquitination appeared to reduce Rab7 function by disrupting its interactions with an effector protein.

These results suggest that *parkin* mutations alter membrane trafficking by reducing Rab7 function. Interestingly, PD-causing mutations in another protein, LRRK2, also reduce Rab7 function (Gómez-Suaga et al., 2014, Hum Mol Genet 23: 6779), supporting the hypothesis that this defect contributes to PD pathology. Why nigral dopaminergic neurons are particularly susceptible to degeneration resulting from such trafficking defects remains to be investigated.

This Week in The Journal is written by Teresa Esch, Ph.D.