Harnessing brain signals to move paralyzed limbs

Engineers have developed remarkable devices that allow patients with paralysis to regain control of hand movements and to achieve a greater measure of independence in daily activities. The technology, called functional electrical stimulation (FES), can already be used to restore movements to paralyzed limbs by directly stimulating muscles.

These systems rely on movement of other parts of the limb that are still functional, such as a shrug of the shoulders, which is not possible in all patients. Furthermore, most systems can only produce one or two types of movements, rather than being able to mimic the complexity of normal hand movements. L.E. Miller and colleagues at Northwestern University (Chicago, IL) have now developed an FES system that can directly use signals from the brain to control movements.

They first trained two rhesus macaques to pick up a ball and put it in a dispenser. After the monkey had learned the behavior, each monkey was implanted with a multi-electrode recording array in the hand area of the motor cortex. More electrodes were implanted in the muscles of the hand and forearm for recording and stimulation.

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While the monkeys were performing the trained behavior, the researchers simultaneously recorded the activity in the hand and arm muscles as well as the neurons in the motor cortex. These recordings were used to build a decoder, which could be used to translate the commands being relayed from the motor cortex to the electrodes to stimulate the appropriate muscles in the arm (*Nature* doi:10.1038/nature10987; published online 18 April 2012).

To test the decoder, they blocked the nerves in the arm and hand to induce temporary paralysis. When the prosthetic equipment was turned off, the monkeys were no longer able to even pick up the ball. When the equipment was turned on, however, the implanted device relayed the messages from the brain to the electrodes in the arm muscles through wires, bypassing the blocked nerves and restoring the monkeys' ability to pick up the ball and put it in the dispenser.

While the model of paralysis used in this study avoided some of the complications of actual spinal cord injury, such as denervation of paralyzed muscles, the scientists hope that their system could be used to help people with spinal cord injuries regain some control over their hands. Miller told *The Scientist*, "There are really no significant technical hurdles that would prevent us from taking this combined technology to humans."

Kara Rosania

REFINING ZEBRAFISH HOUSING FOR MORE RELIABLE RESULTS

Zebrafish are becoming more common as subjects in neuroscience studies of behavior and in screens for new treatments of behavioral disorders such as addiction, attention deficits and autism spectrum disorders. The fish are small and reproduce prolifically, making it easy and relatively affordable to house large numbers of them in the laboratory. In addition, they are amenable to genetic manipulation to study the effects of specific genes on behavior.

A behavior test commonly used to assess stress levels in zebrafish is the tank diving test. A fish placed in a new tank typically dives to the bottom of the tank and hovers there, stationary, for some time before rising. The amount of time the fish spends at the bottom is considered to vary in proportion with its stress level: a longer interval reflects greater stress. Such tests may be used to analyze the efficacy of potential new treatments for anxiety disorders.

In other lab animal species such as rodents, housing and handling procedures are known to affect the results of behavioral experiments, but few studies have examined how husbandry practices may affect results of zebrafish experiments. Caroline H. Brennan and colleagues at Queen Mary University of London (UK) predicted that zebrafish housing environments would affect their stress levels and, therefore, the results of tank diving assays. Overall, they found that individually housed fish exhibited different behaviors on the tank diving test than did group-housed fish (*PLoS ONE* **7**, e34992; 2012). They spent less time on the bottom of the tank than did group-housed fish. Individually housed fish also responded to treatment with ethanol, which has anti-anxiety effects, whereas group-housed fish did not. Finally, levels of the stress hormone cortisol were lower in individually housed fish.

The group concludes that a zebrafish's tank diving response is related specifically to the degree of change from the environment from which the fish had come. This means that housing is an important factor in obtaining reliable data from behavioral tests in zebrafish. Brennan stated in a press release, "Not only will publication of our results improve the reliability of zebrafish behavioural analysis, but, by demonstrating that by refining housing one can increase the power of our analysis and reduce the number of animals used, we contribute to the 3Rs aim of UK and international science policy—to reduce, refine and replace animals in research."

Monica Harrington