Training the brain to overcome deficits

A parent whose baby has a seizure may understandably worry about the long-term effects on the infant's brain. Early-life seizures are known to disrupt neurological development and can lead to cognitive deficits in learning and memory. But a recent animal study from the Department of Neurology suggests that, with enough practice, the brain can compensate for such deficits by increasing communication between two key regions—the hippocampus and the prefrontal cortex.

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Pierre-Pascal Lenck-Santini (left) and M.D.-Ph.D. student Jonathan Kleen study the long-term effects of seizures on the development of the brain.

The hippocampus is responsible for forming short-term memories and making new memories. The prefrontal cortex is home to executive functions—thought processes such as making plans and focusing attention.

"Both structures are affected in epilepsy [and] when you have early-life seizures," explains Pierre-Pascal Lenck-Santini, Ph.D., an assistant professor of neurology and one of the authors of the study, which was published in the *Journal of Neuroscience*.

"Most people with epilepsy are able to lead normal lives despite this," says Jonathan Kleen, an M.D.-Ph.D. student who led the study. "We wanted to find out how the brain might be adjusting itself" to compensate for abnormalities caused by seizures. To do this, Kleen and his colleagues conducted a series of experiments involving rats that had had early-life seizures and rats that had not.

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Edie Wu, a Dartmouth undergraduate, taught the rodents how to perform a variety of tasks, such as poking their nose through a beam of light and then waiting to push a lever in order to get a food reward. The tasks varied in their difficulty and in how much short-term memory was required. Those involving longer delays between steps proved more difficult for the rats that had had early-life seizures. But with extra training, they eventually succeeded.

When rats that had had seizures performed the more complicated tasks correctly, communication between the prefrontal cortex and the hippocampus was much greater than usual.

The prefrontal cortex "seemed to be picking up the slack, so to speak," says Kleen. "It did this by producing stronger electrical brain waves . . . and synchronizing them with waves in the hippocampus."

This suggests that "even though you have a problem in your brain, you can overcome it by increasing the training," adds Lenck-Santini.

It's long been known that with the right therapy and support, people can overcome cognitive disabilities to perform on par with those who do not have difficulty with learning and memory. But until now, no one knew how the brain actually accomplished that.

These findings, although incremental, are an important step along the way to better understanding epilepsy and ultimately finding better treatments for the disease, especially in children.

Kleen, working with Gregory Holmes, M.D., the chair of the Department of Neurology, has already begun translating these results to humans by recording brain activity in DHMC patients with epilepsy while they play computer games designed by the researchers.

"We hope to find compensatory pathways that will be more directly applicable to the human condition," says Kleen. He adds, putting scientific lingo aside, "the brain is just so dang incredible." — Jennifer Durgin