Four studies explore memory decline in people with epilepsy

December 6 2015

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Four studies presented at the American Epilepsy Society's (AES) 69th Annual Meeting uncover the biological factors that mediate memory decline in people with epilepsy, particularly those with seizures that affect the temporal lobe.

Loss of neurons from the hippocampus, a brain region that processes and

stores memories, is a common cause of temporal lobe epilepsy. People with temporal epilepsy caused by hippocampal sclerosis (TLE-HS) have impaired memory and find it particularly challenging to recall details of specific events in everyday life.

In the first study, (abstract 2.326) researchers from the University of São Paulo report that patients with TLE-HS have everyday dramatic memory deficits that may not be detected via traditional neuropsychological tests. Noting the inconsistency between neuropsychological test results, and patient complaints of memory loss in everyday life, the researchers set out to generate a more realistic picture of memory performance in these patients.

Comparisons of cognitive performance in 30 people with TLE-HS and 27 age- and gender-matched healthy participants revealed that patients with TLE-HS were less likely to recall the names of unfamiliar people, places where personal items were stored or detailed stories. Patients with TLE-HS also had difficulty orienting themselves in time and space. The authors further report that cognitive performance was significantly lower in patients with poor seizure control and those taking multiple antiepileptic drugs.

"We found that patients with TLE-HS had deficits in everyday memory functions, including significant impairments in daily activities that are not evaluated in a standard neuropsychological evaluation. These impairments can make it difficult for patients to socially adapt and should receive greater attention in the neuropsychological evaluation of patients with memory complaints. Everyday memory evaluation does not replace the traditional neuropsychological tests, but adds valuable information regarding memory complaints and guide rehabilitation," says author Kette Valente, M.D., Ph.D., a professor in the Laboratory of Clinical Neurophysiology at the University of São Paulo Medical School.

In a second study, (abstract 3.312) researchers from the Federal University of São Paulo show that reduced cell density in certain parts of the hippocampus may be linked to deficits in short- and long-term memory in certain patients with TLE-HS.

The researchers evaluated memory and language in 72 patients with TLE-HS who were undergoing pre-operative evaluation, then examined samples of brain tissue that were removed from the hippocampus during epilepsy surgery. They report that performance on all elements of the neuropsychological tests was worse in patients with degeneration on the right side of the hippocampus compared with the left side.

"Despite the fact that the literature describes only correlation between verbal memory tests and hippocampal cell densities in patients with left hippocampal sclerosis, we found a correlation between right hippocampal cell densities and performance on visual memory tests, including both immediate and delayed recall," says authors Sandra Mara Comper and Anaclara Prada Jardim, students in the laboratory of Dr. Elza Marcia Yacubian at the Federal University of São Paulo.

A third study (abstract 3.244) finds that large brain function networks are affected by focal forms of epilepsy. Researchers from the National Autonomous University of Mexico, the General Hospital of Mexico and Centro Estatal de Salud Mental (CESAM), Queretaro studied patients with temporal lobe epilepsy and healthy participants, using fMRI to monitor brain activity in the cerebral cortex while the groups completed an activity known as Sternberg's task, which assesses working memory. The brain activity was then analyzed along with participants' performance on a neuropsychological evaluation. The groups exhibited similar brain activity despite the observation that patients with epilepsy required significantly longer times to complete the task, and in epilepsy patients (but not in controls) there were specific brain regions that showed a direct relation between their level of activity and the patient's

cognitive performance metrics.

"Our results show that while patients have relatively small deficits in working memory, the activity of the cortical networks that support such a function are predictive of their performance," says author Vicente Camacho, M.D., and a Masters student at the National Autonomous University of Mexico.

A fourth study finds that a generalized seizure leads to diminished short and long-term memory by interfering with key signaling pathways in the brain. It is well known that seizures produce learning, memory and behavioral deficits, and that they trigger abnormally high activity of two signaling pathways in the brain: the phosphoinositide 3-kinase (PI3K) and mechanistic target of rapamycin (mTOR) cascades. But whether abnormal signaling is to blame for these deficits remains unclear.

Researchers from the Baylor College of Medicine and the Gordon and Mary Cain Foundation Laboratories explored the effects of seizure activity on short- and long-term memory in a rat model of epilepsy. The researchers also tested whether learning and memory deficits could be corrected using drugs that calm the overactive signaling cascades. They report that signaling activity remained high 3 hours after a seizure, but returned to normal levels within 24 hours. Seizures induced significant deficits in short as well as long-term memory. The memory deficits that could be partially corrected using the drug wortmannin, which inhibits PI3K and mTOR.

"Studies are underway to reveal how seizures affect various types of memory and to explore the associated molecular signaling and morphological alterations," says author Angela Carter, a predoctoral fellow in the laboratory of Dr. Anne Anderson at the Baylor College of Medicine.

Provided by American Epilepsy Society