What causes seizure in focal epilepsy?

April 13 2010

In focal epilepsy, seizures are generated by a localized, synchronous neuronal electrical discharge that may spread to large portions of the brain. In spite of intense research in the field of epilepsy, a key question remains unanswered: what are the earliest cellular events leading to the initiation of a focal seizure?

Elucidating this issue is of paramount importance both for understanding the pathophysiology of focal epilepsies and for the development of new pharmacological strategies for drug-resistant forms of these disorders. Publishing next week in the online, open access journal PLoS Biology, a new study reveals that early activation of astroglia, the main population of glial cells in the brain, by hyperactive neurons is one of the crucial events that predisposes neurons nearby to the generation of an epileptic discharge.

By monitoring the activity of neurons and astroglia by simultaneous single or dual patch-clamp recordings, field potential recordings, and Ca2+ signal imaging in different experimental models of epilepsy, Giorgio Carmignoto and colleagues at the National Research Council, Italy, found that an episode of hyperactivity in a restricted group of neurons massively activates nearby astrocytes. Activated astrocytes, in turn, signal back to neurons and potentiate hypersynchronized neuronal activity. In conditions of enhanced excitability, this astrocyte feedback signal drives neurons towards the seizure-like discharge threshold. Accordingly, selective inhibition or stimulation of astrocyte Ca2+ signalling reduced or enhanced, respectively, seizure discharge generation. Epileptic discharge, in turn, triggers a second activation of

astrocytes that may favour seizure propagation.

In summary, this study reveals that a recurrent excitatory loop between neurons and astrocytes developing at restricted brain sites promotes and sustains epileptic seizures. This neuron-astrocyte interaction may represent a novel target for the development of effective therapeutic strategies to control epilepsy and target drug-resistant forms of the condition.

More information: Gómez-Gonzalo M, Losi G, Chiavegato A, Zonta M, Cammarota M, et al. (2010) An Excitatory Loop with Astrocytes Contributes to Drive Neurons to Seizure Threshold. PLoS Biol 8(4): e1000352. doi:10.1371/journal.pbio.1000352

Provided by Public Library of Science