Scientific Reports, 2021, vol.11, N1

Proteomic profiling of the rat hippocampus from the kindling and pilocarpine models of epilepsy: potential targets in calcium regulatory network

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Abstract

Herein proteomic profiling of the rat hippocampus from the kindling and pilocarpine models of epilepsy was performed to achieve new potential targets for treating epileptic seizures. A total of 144 differently expressed proteins in both left and right hippocampi by two-dimensional electrophoresis coupled to matrix-assisted laser desorption-mass spectrometry were identified across the rat models of epilepsy. Based on network analysis, the majority of differentially expressed proteins were associated with Ca2+ homeostasis. Changes in ADP-ribosyl cyclase (ADPRC), lysophosphatidic acid receptor 3 (LPAR3), calreticulin, ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), synaptosomal nerve-associated protein 25 (SNAP 25) and transgelin 3 proteins were probed by Western blot analysis and validated using immunohistochemistry. Inhibition of calcium influx by 8-Bromo-cADP-Ribose (8-Br-cADPR) and 2-Aminoethyl diphenylborinate (2-APB) which act via the ADPRC and LPAR3, respectively, attenuated epileptic seizures. Considering a wide range of molecular events and effective role of calcium homeostasis in epilepsy, polypharmacy with multiple realistic targets should be further explored to reach the most effective treatments.

http://dx.doi.org/10.1038/s41598-021-87555-7

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