Activity-dependence of glutamate decarboxylase in dissociated culture of rat hippocampal neurons

Abstract

Imbalances in neuronal activity are often symptoms of diseases such as epilepsy and schizophrenia. However, the mammalian central nervous system can usually avoid these imbalances. When neurons are chronically hyper activated (such as by addition of picrotoxin to cultures), neurons will undergo mechanisms to down regulate their activity at most synapses. The inverse - chronic hypoactivity of an entire population of neurons - will cause upregulation of activity at most synapses. These mechanisms help to avoid such neurological disorders. However, the role of inhibitory neurons in this process, a highly varied and interesting kind of cell in the central nervous system, is not entirely clear. Especially unclear is the localization and expression of glutamate decarboxylase (GAD) - the molecule that is responsible for the conversion of glutamate into the main inhibitory neurotransmitter in the brain - and its role in the process. The control of this hyper- or hypoactivity by GAD is crucial for brain development and maintenance. This thesis aims to elucidate some patterns and characteristics of GAD in neurons under chronic alteration of activity by culture of dissociated rat hippocampal neurons. By measuring fluorescence in immunohistochemical preparations as well as green fluorescent protein (GFP)-tagged GAD in live cultures, I have been able to measure some of these characteristics. The results suggest that the profile of expression of GAD at synapses indeed changes directly in response to alteration of activity. Other data suggest that a mechanism for the rapid modification of the localization of GAD is present but may be independent of activity.