Redistribution of Microtubules in Dendrites of Hippocampal CA1 Neurons after Tetanic Stimulation during Long-Term Potentiation

Fuyuki Mitsuyama [1,6,7,8], Gen Niimi [2], Kunio Kato [3], Kazushige Hirosawa [4], Katsuhiko Mikoshiba [3,5,6], Masato Okuya [7], Kostadin Karagiozov [1], Yoko Kato [1], Tetsuo Kanno [1], Hirotoshi Sano [1] and Tadashi Koide [8]

[1] Department of Neurosurgery, Fujita Health University, Toyoake, Aichi, Japan
[2] Laboratory of Electron Microscopy, Fujita Health University, Toyoake, Aichi, Japan
[3] The Calciosignal Net Project, Exploratory Research for Advanced Technology, Japan Science and Technology Corporation, Bunkyo, Tokyo, Japan
[4] Departments of Fine Morphology, Institute of Medical Science, The University of Tokyo, Minato, Tokyo, Japan
[5] Division of Molecular Neurobiology, Department of Basic Medical Science, Institute of Medical Science, University of Tokyo, Minato, Tokyo, Japan
[6] Laboratory for Developmental Neurobiology, Brain Science Institute (BSI), RIKEN, Wako-shi, Saitama, Japan
[7] Department of Internal Medicine, Tenjyu Hospital, Nagoya, Aichi, Japan
[8] Fukuyu Medical Institute, Nagoya, Aichi, Japan

Key words: microtubules, redistribution, AMPA receptor, receptor trafficking, LTP, learning and memory

SUMMARY

It is now well accepted that the trafficking of AMPA receptors to the postsynaptic plasma membrane plays an essential role in long-term potentiation at the hippocampal Schaffer collateral synapses on CA1 pyramidal cells, but the motor mechanism of trafficking is unknown. We suspected that this trafficking of AMPA receptors during long-term potentiation may be carried out along microtubules by their motors. To ascertain this hypothesis, we light- and electron-microscopically studied the distribution of microtubules in dendrites of CA1 neurons of non-stimulated and stimulated rat hippocampal slices by using very strong tetanic stimulation for inducing long-term potentiation. As a result, we observed the following changes: 1.In immunofluorescence for microtubules and IP_3 receptor using ultrathin-cryosections, linear signals of microtubules in main dendritic shafts were changed into fragmented. 2.Many spotty signals of microtubules emerged at the peripheral area of dendrites. Electron-microscopically, there was redistribution of microtubules in dendritic spines and dendritic shafts, and the thickening of post-synaptic density. 3. Many microtubules concentrated to thickened postsynaptic density in spines and new ones emerged, going to spines from dendritic shafts. These results strongly suggest that new tracks of microtubules from cell bodies to the stimulated postsynaptic membranes were produced after tetanic stimulation during long-term potentiation. This newly produced microtubules between stimulated postsynaptic membranes and the cell body must be the most promising candidate of the track for the trafficking of AMPA receptors to the stimulated postsynaptic plasma membrane.