Menahem Segal

Miri Goldin
Varda Greenberger
Ariel Kamsler
Edi Korkotian
Natalie Landman
Yair Pilpel

Morphological and functional plasticity in central neurons

Department of Neurobiology

Tel. 972 8 934 2553 **Fax.** 972 8 934 4140
E-mail: menahem.segal@weizmann.ac.il

Morphological and functional aspects of neuronal plasticity are studied in networks of cultured neurons taken from rodent brains, or in brain slices from adult rats/mice. Using dye-or GFP loaded neurons in a confocal microscope, we study morphological changes in dendritic spines of the cultured neurons following exposure of the culture to stimulation that produce sustained changes in network activity of these neurons. The sequence of molecular and morphological events that lead to the formation of novel synapses are studied. The involvement of MAP-Kinases and cyclic AMP response element binding protein (CREB) has been documented. Dendritic spines of cultured hippocampal neurons express local motility that depends on actin polimerization, and can even twitch in response to a sudden rise in intracellular calcium concentration, occuring, for example during a back propagating action potential. The function of spine movements in the establishment of connections among neurons are analyzed. The functional connection between the dendritic spine and its parent dendrite is studied with fast calcium imaging in the confocal microscope. We found that the length of the spine is extremely important in the communication of calcium signal between the spine and the dendrite. Using focal stimulation with pulsed laser to uncage glutamate, we evoke local responses in the spines, and study their communication with the parent dendrite. Using transfection methodologies, we study the role of individual molecular species in formation of functional synapses among neurons.

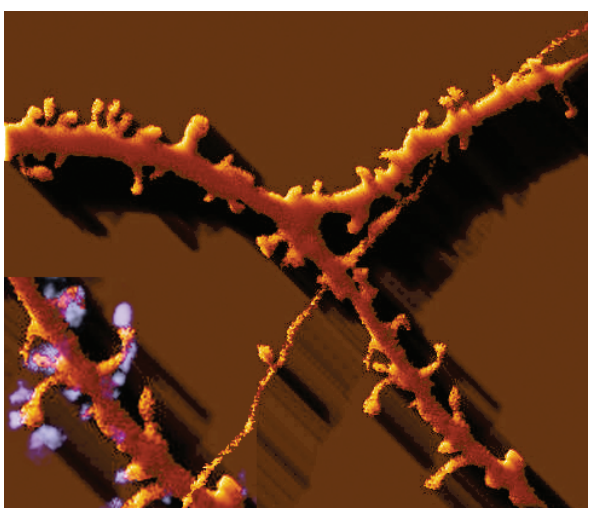

Fig. 1 *Reconstruction of dendritic spines in cultured hippocampal neurons on a confocal laser scanning microscope. Bottom left, a segment of a dendrite, counterstaind with FM4-64 to demonstrate presynaptic terminals on the dendritic spines.*

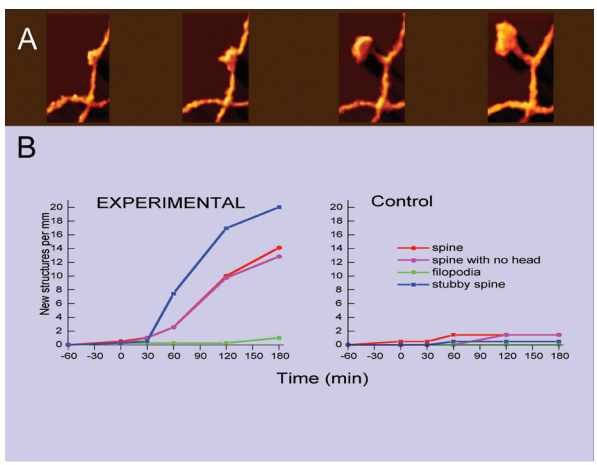

Fig. 2 *Formation of novel spines in cultured neurons (From Goldin et al, 2001).*

The role of oxidative stress in neuronal plasticity is studied in brain slices taken from transgenic SOD overexpressing mice, and in brain slices of rats that are exposed to hydrogen peroxide. A dual action of H_2O_2 in long term potentiation has been demonstrated. These studies address fundamental issues in neuronal plasticity and in the relation between structure and function of central neurons.

Selected Publications

Golan H., K. Mikenberg, V. Greenberger and M. Segal (2000) GABA withdrawal modifies network activity in cultured hippocampal neurons. Neuronal Plasticity 7, 31-42. .

Segal, M. E. Korkotian, and D. D. Murphy (2000) Dendritic spine induction and pruning- common cellular mechanisms? Trends in Neuroscience 23, 53-57.

Segal M and P. Andersen (2000) Dendritic spines shaped

by synaptic activity. Current opinions in Neurobiology 10, 582-587.
Braun K. and Segal M. (2000) FMRP involvement in formation of synapses among cultured hippocampal neurons. Cerebral Cortex 10, 1045-52.
Korkotian E. and Segal M. (2000) Structure-function relations in dendritic spines: Is size important? Hippocampus 10, 587-595.
Murphy D. and Segal M. (2000) Progesterone prevents estradiol-induced dendritic spine formation in cultured hippocampal neurons. Neuroendocrinology 72, 133-143.
Levkovits Y. and M. Segal (2000) Aging affects transcranial magnetic modulation of hippocampal evoked potentials. Neurobiol. Aging 22, 255-263.
Goldin M. Segal M and E. Avignone (2001) Functional plasticity triggers formation and pruning of dendritic spines in cultured hippocampal networks. J. Neuroscience 21, 186-193.
Segal M. (2001) Rapid plasticity of dendritic spines: hints to possible functions? Prog. Neurobiol. 63, 61-70.
Levkovitz Y and M. Segal (2001) Transcranial Magnetic Stimulation and antidepressive drugs share similar cellular effects in rat hippocampus. Neuropsychopharmacology.24:608-616.
Collin C., Vicario-abejon C., Rubio, M.E., Wenthold R.J. McKay R.D.G, and M. Segal (2001) Neurotrophins act at pre-synaptic terminals to activate synapses among cultured hippocampal neurons. European J. Neuroscience 13, 1273-1282.
Segal M. and D Murphy (2001) Estradiol induces formation of dendritic spines in hippocampal neurons: functional correlates. Hormones and Behavior 40, 156-159.
Korkotian E. and Segal M. (2001) Spike-associated fast twitches of dendritic spines in cultured hippocampal neurons. Neuron 30, 751-758.
Korkotian E. and Segal M (2001) Regulation of dendritic spine motility in cultured hippocampal neurons. J. Neuroscience 21: 6115-6124.

Acknowledgements

Research in our lab is supported by grants from BSF, Volkswagen Foundation, Alzheimers Association, FRAXA, EC and Ministry of Science.

M.S. holds the Harry and Leona Levine Chair of Neurosciences.

For additional information see:

www.weizmann.ac.il/neurobiology/labs/segal/segal.html