

Recent Advances in Network Electrophysiology Using Multi-Electrode Arrays

Monday, November 10, 2003. 6:30 pm – 9:00 pm
Convention Center, Room 253, New Orleans, LA

Rapid Modulation of Hippocampal Neuronal Plasticity by Brain Estrogen and Endocrine Disrupters (Eds): an Electrophysiological Analysis

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Electrophysiology is one of the most sensitive method to detect the acute effect of neurosteroids on learning and memory. The acute actions of estradiol, and EDs (e.g., bisphenol A (BPA) and diethylstilbesterol (DES)) were analyzed by measuring the longterm potentiation (LTP) induced upon titanic stimulation of the CA1 pyramidal neurons in rat hippocampal slices. A 30 min preperfusion with 10 nM estradiol enhanced the LTP in 4 and 12 weekold rats. Application of 10 nM DES had an almost identical enhancing effect on LTP to that obtained by estradiol. Both effects were completely suppressed by ICI 182,780, an ER α inhibitor. On the other hand, coapplication of 100 nM BPA and 10 nM estradiol considerably suppressed the estradiolinduced enhancement of LTP, although application of BPA alone, even at 100 nM, did not significantly affect LTP. These findings suggest that EDs do have significant disrupting actions on learning and memory, and that their enhancing/suppressive effects are depending on individual EDs.

It should be noted that estrogens are locally synthesized de novo in the hippocampus, independent of peripheral estrogens from blood circulation. Therefore, brain-derived estrogens can act as local messengers. We demonstrated the Ca²⁺-driven synthesis of estrogens in rat hippocampal neurons. In pathway of neurosteroidogenesis, cholesterol is converted to pregnenolone, dehydroepiandrosterone, androstenedione, testosterone and finally to estradiol. Co-localization of steroidogenic enzymes (such as cytochromes P450_{scc}, P450_{17 α} , P450_{arom}) was observed in pyramidal and granule neurons in the CA1-CA3 and DG, by using immunohistochemical staining and immunoelectron microscopy of hippocampal slices.

References

1. S. Kawato, et al., in *Methods in Enzymol.* (2002) Vol. 357, 241-249 "Histological and Metabolism Analysis of P450 in Brain"
2. K. Shibuya, et al., *Biochim. Biophys. Acta* (2003) 1619, 301-316 "Hippocampal cytochrome P450s synthesize brain neurosteroids which are paracrine neuromodulators of synaptic signal transduction"
3. Y. Hojo, Y., et al., *Proc. Natl. Acad. Sci. U.S.A.*, in the press (2003) "Adult male rat hippocampus synthesizes estradiol from pregnenolone by cytochromes P450_{17 α} and P450_{arom} localized in neurons."
4. S. Kawato, *Environmental Sciences*, in the press (2003) "Endocrine disrupters as disrupters of learning and memory in the brain: from the viewpoint of neurosteroid"