Synaptic plasticity in NCS-1 knock-out and NCS-1-EGFP overexpressing mice

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Neuronal calcium sensor 1 (NCS-1) has an important role in synaptic plasticity. For example, increases in NCS-1 protein concentration in cultured hippocampal neurons can switch short-term plasticity from paired-pulse depression (PPD) to paired pulse facilitation (PPF). Recently it was shown that functional knock-down of NCS-1 impairs metabotropic glutamate receptor dependent long-term depression (mGluR-LTD) in perirhinal cortex from newborn rats [1]. This form of mGluR-LTD is thought to promote AMPA receptor internalization involving a PICK-1 and NCS-1 dependent Ca^{2+}-signaling mechanism.

In order to better define the physiological role of NCS-1 in mGluR regulated vesicular trafficking of ion channel protein we have generated NCS-1 knock-out (KO) and transgenic mouse lines expressing NCS-1-EGFP fusion protein (TG). We have begun to investigate effects of loss or gain of NCS-1 function on synaptic plasticity in mouse brain. The NCS-1 KO as well as TG animals show no gross behavioral phenotype and have normal appearance, body weight and life expectancy.

Electrophysiological recordings of field excitatory postsynaptic potentials (fEPSP) in hippocampal slices showed altered short term plasticity at hippocampal synapes of mice with altered NCS-1 protein expression. We recorded PPF at perforant path synapses in dentate gyrus as well as in the CA1 region of hippocampus. The results showed markedly reduced PPF in TG animals in comparison to wildtype controls. This data will be compared to results obtained from hippocampal slices of NCS-1 KO mice.

[1] Jo J. et al. Neuron (2008), 60(6): 1095-1111