Neuroscience Colloquium

Winter Semester 2017/2018

Lectures are held Thursdays, 5 p.m.
Venue: Paul-Ehrlich Lecturehall, Virchowweg 4, next to CCO

Chris McBain

NIH AND EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT, SECTION ON CELLULAR AND SYNAPTIC PHYSIOLOGY – NEUROSCIENCES, BETHESDA, USA

Glutamate receptors control GABAergic Inhibitory interneuron cell and circuit maturation.

Circuit computation requires precision in the timing, extent, and synchrony of principal cell firing that is largely enforced by parvalbumin-expressing, fast-spiking interneurons (PVFSIs). To reliably coordinate network activity, PVFSIs exhibit specialized synaptic and membrane properties that promote efficient afferent recruitment such as expression of high-conductance, rapidly gating, GluA4-containing AMPA receptors. We found that PVFSIs upregulate GluA4 during the second postnatal week coincident with increases in the AMPAR clustering proteins NPTX2 and NPTXR. Moreover, GluA4 is dramatically reduced in NPTX2(-/-)/NPTXR(-/-) mice with consequent reductions in PVFSI AMPAR function. Early postnatal NPTX2(-/-)/NPTXR(-/-) mice exhibit delayed circuit maturation with a prolonged critical period permissive for giant depolarizing potentials. Juvenile NPTX2(-/-)/NPTXR(-/-) mice display reduced feedforward inhibition yielding a circuit deficient in rhythmogenesis and prone to epileptiform discharges.

Memory loss in Alzheimer's disease (AD) is attributed to pervasive weakening and loss of synapses. In a mouse model of AD amyloidosis, Nptx2-/- results in reduced GluA4 expression, disrupted rhythmicity, and increased pyramidal neuron excitability. Postmortem human AD cortex shows profound reductions of NPTX2 and coordinate reductions of GluA4. NPTX2 in human CSF is reduced in subjects with AD and shows robust correlations with cognitive performance and hippocampal volume. These findings implicate failure of adaptive control of pyramidal neuron-PV circuits as a pathophysiological mechanism contributing to cognitive failure in AD. Our findings demonstrate an essential role for NPTXs in controlling network dynamics highlighting potential therapeutic targets for disorders with inhibition/excitation imbalances such as schizophrenia and (AD).

Location: Paul Ehrlich-Hörsaal,
Charité – Universitätsmedizin Berlin, Campus Mitte
Virchowweg 4, next to CCO

Date: **Thursday, December 7th, 5 p.m.**

Host: Imre Vida

The Neuroscience Colloquium is supported by:
DZNE e.V. German Center for Neurodegenerative Diseases;
Einstein Center for Neurosciences; **NeuroCure** Cluster of Excellence.
Organized by NeuroCure and Institute for Neurophysiology: Christian Rosenmund;
Contact: heidi.pretorius@charite.de