discovering that MTs routinely polymerize into spines in an activity-dependent manner, throughout the life of the neuron. However, the precise role of MT invasion in spine maintenance and plasticity remains unknown. Therefore, we have designed a DNA plasmid construct that targets a MT elimination motif to dendritic spines in a spatially and temporally controlled manner. We have confirmed appropriate localization and MT-depolymerizing activity in cultured hippocampal neurons. Importantly, this construct appears to preserve typical MT dynamicity within the dendritic shaft of transfected neurons. We hypothesize that MT invasion of dendritic spines is critical for molecular remodeling of activated synapses and have begun to quantify effects of MT inhibition on dendritic spine morphology in both activated cultures and those at basal levels of activity. Thus, we have developed a methodology to interrogate the function of MTs throughout dendritic spine development and plasticity with specificity that bath application of pharmacological agents does not allow.

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Topic: AS06 Neural Excitability, Synapses and Plasticity

LONGITUDINAL ACTIN FILAMENTS IN THE AXON INITIAL SEGMENT

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The location of the axon initial segment (AIS) at the junction between the soma and axon of neurons makes it instrumental in maintaining neural polarity and as the site for action potential generation. Our recent results showed that the actin cytoskeleton is involved in the maintenance of AIS structure. Since their discovery by 2013, actin rings of AIS have been broadly studied, but other actin structures, such as the newly identified longitudinal actin filaments here, have gained less attention. Here we used pharmacological treatments and super-resolution microscopy to characterize the longitudinal actin filaments in the AIS. While actin filaments in actin rings are relatively stable and persistent to actin monomer sequestering drugs, longitudinal actin filaments were cleared from AIS by these drugs, indicating that actin filaments in longitudinal actin filaments are dynamic. By inhibiting formin polymerization, we could reduce the presence of longitudinal actin filaments in the AIS, suggesting that formins play a role in their polymerization. In line with this, we observed that one of the formins, Daam1, localizes in the ends of longitudinal filaments. Presence of longitudinal actin filaments was increased during AIS plasticity and general formin inhibition blocked the structural changes occurring during AIS plasticity. In summary, we identified novel actin structures in the AIS which seem to contribute to AIS structural plasticity.

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Topic: AS06 Neural Excitability, Synapses and Plasticity

IDENTIFICATION OF NON-EXCITATORY AMINO ACIDS AND TRANSPORTERS MEDIATING THE IRREVERSIBLE SYNAPTIC SILENCING AFTER HYPOXIA

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The contribution of excitatory amino acids (AA) to ischemic brain injury has been widely described. In addition, we reported that a mixture of non-excitatory AA at plasmatic concentrations turns irreversible the depression of synaptic transmission caused by hypoxia. We describe that the presence of seven non-excitatory AA (L-alanine, L-glutamine, glycine, L-histidine, L-serine, taurine and L-threonine) during hypoxia provokes an irreversible neuronal membrane depolarization, after an initial phase of hyperpolarization. The collapse of the membrane potential correlates with a huge increase in FV amplitude. Nevertheless, we show that the presence of those seven AA is not necessary to cause the irreversible loss of fEPSP after hypoxia and that the minimal combination of AA able to provoke a solid replicable effect is AGQS (L-alanine, glycine, L-glutamine and L-serine). Additionally, L-glutamine seems to be necessary but not sufficient to induce these deleterious effects. We also prove that the deleterious effects of the AA mixtures on field potentials during hypoxia depend on both the identity and concentration of the individual AA in the mixture. Furthermore, we find that the accumulation of AA in the whole slice does not determine the outcome caused by the AA mixtures on synaptic transmission during hypoxia. Finally, results obtained by using inhibitors and specific substrates of AA transporters suggest that system N, ASCT2 and Asc-1 participate in the non-excitatory AA-mediated deleterious effects during hypoxia.

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Topic: AS06 Neural Excitability, Synapses and Plasticity

UNDERSTANDING FNIRS AS A NEUROMODULATORY TECHNIQUE

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Functional Near-Infrared Spectroscopy (fNIRS) is a neuroimaging technique that measures cortical activity by using near-infrared light to monitor changes in tissue oxygenation. Although fNIRS has been used as a measurement tool for decades, recent studies suggest that it may also be capable of modulating neural activity through photobiomodulation (PBM). To investigate the neuromodulatory potential of fNIRS, this study was conducted on 30 healthy participants using

cognitive tests designed to measure prefrontal functioning; the Backwards Counting Task (BCT), Delayed Matched to Sample Task (DMS) and the eStroop. The study found that turning on a device classically used for fNIRS can lead to a modulation in cognitive performance in healthy adults, as shown by better response times in the post-session of the BCT and in the post-session of almost all eStroop conditions. It also found that the fNIR light stimulation received by the experimental group brought about a significant increase in the speed these participants responded, which improved accuracy during the incongruent condition. It suggests that the fNIR light stimulation could stimulate the DLPFC and its involvement may be responsible for the better performance at the eStroop task. The study also found that the fNIR light stimulation produced faster response times in the experimental group during BCT tasks. These results indicate that the use of fNIRS as a measurement tool may have a neuromodulatory impact on cognition. However, further research is needed to fully understand the potential and limitations of fNIRS for neuromodulation.

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Topic: AS06 Neural Excitability, Synapses and Plasticity

PREGNENOLONE SULFATE PROMOTES DENDRITIC FIELD EXPANSION OF CORTICAL CULTURED NEURONS

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Impairments of N-methyl-D-aspartate receptor (NMDAR) activity have been implicated in several neuropsychiatric disorders, with pharmacological inhibition of NMDAR-mediated currents and associated neurobehavioral changes considered as a model of schizophrenia. Evidences from postmortem studies show an alteration in morphology and density of postsynaptic elements in cortical tissue in schizophrenia. While ketamine, phencyclidine and another exogenous antagonist of NMDAR have been used as pharmacological approach for inducing NMDAR hypofunction, little attention has been paid to the endogenous modulators of NMDAR, which emerge to be dysregulated in patients with schizophrenia. We analyzed the effects of brief and long-term exposure of rat cortical cultures to the most prevalent endogenous modulators of NMDAR (kynurenic acid, pregnenolone sulfate, spermidine, and zinc) on neuronal viability, stimulation-induced release of glutamate, and dendritic morphology with synaptic density. Both, glutamate release and neuronal viability studies revealed no difference between the test and control groups. No differences were also observed in the number of dendritic branching and length, primary branches, branch points and neuronal soma size. Comparison of the extent of dendritic projections and branching patterns, however, revealed enhanced distal arborization with the expansion of the dendritic area under prolonged treatment of cultures with pregnenolone sulfate. Also, pregnenolone sulfate had a tendency of increased BDNF expression after brief and long-term exposure. Measurements of the density of glutamatergic synapses showed consistency across all neuronal groups, except those treated with pregnenolone sulfate, which showed a reduction of PSD-95 puncta density. Overall, our data suggest that constitutive glutamatergic activity mediated by pregnenolone sulfate controls the dendritic field expansion and can influence the integrative properties of cortical neurons.

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Topic: AS06 Neural Excitability, Synapses and Plasticity

TONIC GABAA RECEPTOR - MEDIATED INHIBITION IN THE NEOCORTICAL SOMATOSTATIN-EXPRESSING INTERNEURONS.

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Tonic GABAA inhibition is mediated by extrasynaptic GABAA receptors and plays an important role for the excitability of mammalian neocortex. However, little is known about the cell-type specific expression of tonic inhibition in particular types of neocortical interneurons. Somatostatin (SST) - expressing interneurons are one of the subpopulation of GABAergic interneurons (GABA, Gamma-aminobutyric acid). Previous literature study has indicated the lack of tonic inhibition in SST interneurons in the frontoparietal cortex of mice. The aim of the study was to answer the questions whether layer 2/3 SST interneurons in the barrel cortex (the part of primary somatosensory cortex) of mice express tonic GABAA inhibition and how GABA controls intrinsic excitability of these interneurons. Whole-cell patch-clamp method was used in acute brain slices prepared from transgenic mice with fluorescently labeled SST interneurons. A tonic current was analyzed in layer 2/3 SST interneurons and neighboring pyramidal neurons. We observed that layer 2/3 SST interneurons showed the tonic current in response to the GABAA receptor blocker (picrotoxin). This current was comparable to the tonic current measured in layer 2/3 pyramidal neurons. Next, we found that SST interneurons were also sensitive to the delta-subunit selective GABAA receptor agonist (THIP). Finally, we found that picrotoxin reduced the rheobase of evoked spikes in SST interneurons. Altogether, our study indicates that layer 2/3 SST interneurons in the barrel cortex express GABAA tonic inhibition that is delta-subunit dependent and intrinsic excitability of these interneurons is suppressed by GABA. Funding: National Science Centre, Poland OPUS grant 2020/39/B/NZ4/01462 to JUC.

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