Juan BURRONE
MRC Centre - Developmental Neurobiology
King's College London - England

Activity dependent development of axo-axonic synapses along the axon initial segment

Pan Vazquez, Alejandro1; Wefelmeyer, Winnie1; Burrone, Juan1

1.Centre for Developmental Neurobiology, MRC Centre for Neurodevelopmental Disorders, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

The axon initial segment (AIS) is an axonal structure close to the soma with a high density of sodium and potassium channels that defines the site of action potential generation. In principal cells of the cortex, it is also innervated by inhibitory synapses formed by a specific type of GABAergic interneuron, the Chandelier cell. Previous work in the lab has focused on activity-dependent forms of plasticity of the AIS and its synapses (Grubb and Burrone, Nature, 2010; Wefelmeyer et al., PNAS, 2015). Here, we present data characterising the changes these structures undergo during postnatal development in the rodent neocortex and the role that local cortical activity plays in this process. We used a recently developed inducible Cre mouse line, Nkx2.1-CreER, to label Chandelier cell interneurons (Taniguchi et al., Neuron 2011). By visualising Chandelier cell axons and their synaptic boutons in the somatosensory cortex *in vivo*, as well as in fixed brain preparations, during development, we uncovered a narrow temporal window of synapse formation at the AIS (from P14-P16). We then manipulated the activity levels of either pyramidal neurons or individual Chandelier cells during this period of synapse formation, using a chemogenetic approach. We found that increases in the activity of cortical networks results in a reversible decrease in the length of the AIS as well as the number of axo-axonic synapses it received. Increasing activity specifically in Chandelier cells mirrors the synaptic effect, suggesting this plasticity is cell autonomous. Importantly, no effect was observed when increases in network activity were induced in adult animals (P40), suggesting a critical window for the plasticity of ChC synapses during development. We are currently characterising the functional consequences of these activity-dependent forms of plasticity on network function to better understand the role Chandelier cells play in microcircuit formation.