SYNAPSE-GLIAL INTERACTIONS IN REGULATION OF NETWORK DYSFUNCTION UNDERPINNING COGNITIVE IMPAIRMENT

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In their preclinical phase, patients affected by a wide range of dementia-related pathologies like Alzheimer's disease or age-related dementia, present with some degree of (mild) cognitive impairment (MCI). An emerging hypothesis is that MCI is just the readout of a variety of disease causes which, independently of their combination, culminate in the disruption of the excitatory vs. inhibitory balance (EIB) of neural circuits. Nonetheless, neither sites of this disruption nor details of the causative signaling pathways are completely identified. Neuron-glial interactions at synaptic loci have come under the spotlight of modern neuroscience research insofar as they could constitute a common link between multiple causes of MCI with the potential to evolve our understanding of etiology of multiple MCI-associated pathologies. Among the candidate mechanisms is the possibility that astrocytes and oligodendrocytes – the main glial cell types in the cortex – could regulate neural excitability and synaptic transmission of neuronal ensembles in a concerted fashion, both in space and time. Based on these arguments, a theoretical framework is discussed which predicts critical roles for synaptic-glial interactions in emergence and death of hyperexcitability of cortical networks. Furthermore, it is revealed how glial could perturb the EIB both locally and globally by accounting for multiple states of synaptic release which, depending on environmental constraints, could ultimately result in seemingly aberrant patterns of neural activity, that closely resemble neural correlates of MCI.