On the road map of astrocyte functional heterogeneity: implications in sensory processing and spontaneous activity

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Astrocytes, the main glial cell type in the central nervous system, are now recognized as integral participants of every major aspect of brain development, function and disease. Traditionally viewed as a largely homogenous population, recent genetic and molecular data mostly obtained from different cortical layers, indicate astrocytes as heterogenous cells in terms of morphology, physiology and gene expression patterns. If such heterogeneity plays a role in the unique patterns of neuronal activity engaged during both spontaneous and sensory-driven responses across different cortical layers is still unknown. By using genetic and pharmacogenetic tools combined with calcium imaging, *in vivo* electrophysiology and behavior assessment in mice, here we will present new data regarding two unanswered questions: 1) are astrocytes functionally heterogenous across distinct layers from the same cortical column? and 2) does astrocyte heterogeneity interfere in the control of spontaneous and evoked layering excitability? Our data shows, for the first time, that astrocyte activity is inherently distinct across layers of the somatosensory cortex. Such diversity seems to play a role in the fine-tuning of evoked neuronal responses by modulating stimulus sensitivity in a layer-dependent manner with consequences to sensory discrimination and behavior output. Regarding spontaneous activity, astrocytic activation seems to desynchronize neuronal activity within slow wave oscillations with subsequent elongation of up-states. In addition, astrocyte activation awakens a subset of inhibitory neurons whose spiking activity is mostly found during down-states. This effect was only evident in layer 5 neurons, showing a layer-specific control of astrocytes in the layer considered as the main generator of spontaneous cortical activity. Therefore, our overall data demonstrate that astrocytes are functionally heterogenic across cortical layers and that such layer-specific differences play important roles in the regulation of sensory processing as well as the neuronal network controlling slow wave oscillations.