3-S30-4 Symposium30

Looking into glial power in regulation of mood disorders

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It is now well understood that astrocytes intimately interact with neurons to support and regulate their functions in many aspects. One of most discussed functions of astrocytes concerns their role in extracellular potassium spatial buffering. A wealth of investigations has focused on the astroglial-neural interactions at the tripartite synapses, where astrocyte processes tightly wrap around pre- and post-synaptic sites. In contrast, not as much attention has been placed on astroglial-neural interaction in proximity to neuronal soma. Particularly, how astrocytes regulate intrinsic firing patterns of neurons, and what structural basis may underlie this regulation, are much less explored. Here we demonstrated the level of Kir4.1 on astrocytes tightly regulates the degree of membrane hyperpolarization and the amount of burst activity of lateral habenular (LHb) neurons. Astrocyte-specific overexpression of Kir4.1 in LHb drives more neuronal bursting and causes depressive-like symptoms. Conversely, knocking down Kir4.1 or overexpression of its dominant negative form in LHb reduces neuronal bursting and ameliorates behavioral despair and anhedonia. Together, we revealed a new form of glial-neural interaction in setting neuronal firing mode in a devastating psychiatric disease, and discover the therapeutic potential of targeting LHb Kir4.1 for treating major depression.