IJAE
Vol. 123, n. 1 (Supplement): 214, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Daily fluctuation of Glia

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We recently reported that the excitatory/inhibitory balance of the innervation of neurons which contain the orexin/hypocretin peptides, located in the lateral hypothalamus, undergoes a remarkable process of daily rearrangement in basal conditions in mice during the periods of the animals' sleep and wake. This finding raises many questions on the regulatory mechanisms. The hypothesis was here tested that daily neuroplasticity could implicate glial cells, since, in the brain, astrocytes are notably key partners of neurons at the synaptic level, and microglia continuously extend and retract their ramifications contacting also synapses. For the present study, unperturbed adult mice and rats were sampled during the day (the period of predominant sleep in these nocturnal animals, as also assessed here with videorecording) or night. In mice, glial cells surrounding orexin neurons were investigated in the lateral hypothalamus. Astrocytes were visualized using glial fibrillary acidic protein as a marker. CX3CR1-GFP mice, in which microglial cells are tagged with green fluorescent protein, were used for the study of microglia. Diurnal changes in microglial morphology and microglia-synapse interactions were investigated in confocal microscopy with multiple immunofluorescence. Three-dimensional reconstructions of glial cells in the lateral hypothalamus revealed striking variations in relation to vigilance state. Astrocytes showed a bushy phenotype, with dense filling of the neuropil, and microglial cells were endowed with highly ramified processes especially at night, when the animals were predominantly awake. Interactions between astrocytic and microglial processes and synapses have been observed during both day and night, and the analysis and quantification of these contacts are currently in progress. Furthermore, to test the activity of microglial cells, microglia-derived microvesicles were quantified in the cerebrospinal fluid of rats, sampled at two time points in antiphase as above. These microvesicles turned out to be significantly more numerous during the period of animals' predominant activity and wakefulness than during the period of predominant rest and sleep. Altogether these sets of data reveal a diurnal fluctuation of the morphology of glial cells in the lateral hypothalamus and of the activity of microglia over the course of the day, opening novel questions on their dynamic properties in relation with behavioural output in health and disease.