Region-specific astrocyte alterations underlie chronic stress response in male mice.

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Major depressive disorder (MDD) is a severe neuropsychiatric illness. Alterations of the blood-brain barrier (BBB), formed by endothelial cells, pericytes and astrocytes, are observed in individuals with MDD and after exposure to chronic social defeat stress (CSDS), a mouse model of depression. Astrocytic morphological changes such as reduced end-feet coverage of blood vessels, occur in the MDD brain and are associated with inflammation and impaired function of these glial cells. However, possible contribution to MDD pathogenesis and maladaptive stress responses remain to be determined. Male mice were subjected to 10-day CSDS producing two subpopulations: stress-susceptible (SS) animals which are characterized by depression-like behaviors and resilient (RES) mice behaving like unstressed controls. CSDS induces BBB hyperpermeability in a region-specific manner, leading to infiltration of inflammatory mediators and development of depressive-like behaviors in SS but not RES animals. Reduced gene expression of connexin gap-junctions, linking neuronal and vascular activity, was noted in the nucleus accumbens of SS male mice, a hub for reward and mood regulation. Conversely, increased expression of growth factors was observed in the prefrontal cortex of RES animals, suggesting compensatory mechanisms in this brain region important for decision making and social behaviors. Functional measurements are ongoing to better define the role of astrocytes in the development of depression-like vs proper stress-coping behaviors. Together, these results suggest that astrocytes could actively contribute to susceptibility vs resilience to chronic stress exposure, and possibly MDD, in a brain region-specific manner.