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Inflammation driven astrocyte responses during neuroinflammation caused by chronic methamphetamine exposure

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Astrocytes provide physical and metabolic support for neurons, control the blood brain barrier, and regulate crucial neurotransmitters. When CNS homeostatic levels are disrupted, astrocytes become reactive. It is unknown if reactive astrocytes are beneficial or detrimental to the system. By studying chronic CNS inflammation, we can begin understanding the role reactive astrocytes play in neurological disorders. Chronic inflammatory disease is recognized as the most significant cause of death in the world, where drug misuse has been a key correlative factor. Chronic abuse of methamphetamine is a leading cause of overdose deaths in California and is a public health problem worldwide. Utilizing flow cytometry to analyze integrin expression, we determined there is inflammation-induced astrocyte heterogeneity based on astrocytic expression of CD51, CD63, and CD71 throughout methamphetamine exposure in mice. Single cell RNA sequencing revealed diverse sub clustering of astrocytes throughout various stages of drug exposure, identifying inflammatory responsive populations. Gene ontology and DEG analysis reveal astrocyte functional changes over the course of meth exposure. Results revealed GLT-1 and vasculature dysregulation, and a specific set of astrocytes highly enriched for APOE found to be involved with potential detrimental enrichment of amyloid fibril formations. Comparison with previously published single cell datasets of other neuroinflammation models, such as Alzheimer's, reveal overlapping and specific populations related to chronic inflammation. Our study contributes to an overarching picture detailing conserved astrocyte functions in various inflammatory environments. These findings have broad implications for astrocytic contributions to drug-induced neurological disease progression, aiding in potential therapeutics for inflammation-related CNS diseases.