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Machine learning analysis of astrocytes in Sharpin mutation mouse model.

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Astrocytes are a type of glial cell that play key roles in maintaining homeostasis of neuronal circuits, regulating neuronal activity, and modulating inflammation. Alzheimer's disease (AD), a common neurodegenerative disorder in the elderly, is characterized by amyloid beta plaques and tau tangles. The chronic inflammation observed in AD is mediated by glial cells including astrocytes, which not only exacerbate disease progression but also lead to a decline in their original glial cell functions. GWAS (Genome-wide association studies) on East Asian AD patients have most prominently observed an association between Sharpin mutations and brain shrinkage. Sharpin is a synaptic protein that binds to the Shank family and is also a component of LUBAC, which regulates NF-κB activity, suggesting its role in synaptic function and inflammation regulation. To investigate the impact of Sharpin mutation-induced changes in the inflammatory response on astrocyte activation, we observed the morphological changes in astrocytes in Sharpin mutant mice comparing to wild-type. Precise quantification of astrocyte activity is challenging and recent research has been attempting to automate microscopic image analysis and classification of them. In this study, we adapted one of those newly developed machine learning algorithms called "Morphious"and optimize it to analyze astrocytes in our mouse models. The optimized machine learning system learned the difference of astrocytes from wildtype and AD model mice. Afterward, Sharpin mutant mouse brains were tested to analyze the impact of the Sharpin mutation on astrocytes. We also measured the number of processes, process length, and stained area of astrocytes using automated batch image processing to characterize astrocyte activation regulated by Sharpin.

Keyword : Alzheimer's disease, Sharpin, Morphious

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