MedicalXpress

New role for glial cells during neuroinflammation

December 17 2013

Astroglial cells in the adult brain play fundamental roles in supporting neuronal functioning and in regulating brain energy balance. A new study now has identified key regulators that allow astrocytes to keep their mitochondrial network functional during neuroinflammation, a condition commonly associated to a variety of brain diseases.

By directly interacting with neuronal synapses and blood vessels, a specialized type of glial cells – the astrocytes – play pivotal roles in sustaining energy metabolism in the healthy brain. In contrast, in most brain pathologies characterized by inflammation, astrocytes enter a reactive state (astrogliosis) resulting in major morphological and metabolic alterations. This form of plasticity may reveal to be an essential aspect of most brain diseases as a failure in regulating astrocyte reactivity during an inflammatory process may worsen the pathology and eventually accelerate neurodegeneration.

Joining their efforts, a team of researchers from the LMU, the University of Cologne and the University of Bologna (Italy), can now offer new insights into the metabolic processes taking place in damaged brain tissue. "Dissecting the metabolic changes that underlie astrogliosis may reveal essential insights which can help us explaining how the brain reacts to injuries and perhaps even offer potential targets for strategies aimed at protecting neurons during neuroinflammation" explain Elisa Motori, first author of the paper, and Matteo Bergami, until recently Research Excellence Fellow at the LMU (Physiological Genomics) and now group leader at the Cluster of Excellence CECAD (Cologne).

To date it has been assumed that nervous system cells react uniformly to acute brain damage such as that caused by traumatic injury. However, Bergami and his co-workers discovered that astrocytes within different zones of the lesion show different forms of reactivity in response to inflammatory insults. This reactivity especially affects mitochondria, the powerhouse of the cells. The function of mitochondria is strictly dependent upon two types of dynamics: fusion and fission. These two reactions are the key for maintaining mitochondrial architecture and function. Faulty regulation of these mitochondrial dynamics results in defective mitochondria, which can lead to cellular aging and trigger many neurodegenerative diseases.

In this study researchers were able to show that astrocytic mitochondria within the core of the damaged, highly proinflammatory brain area, demonstrate an accelerated tendency towards fission, leading to their fragmentation. In the surrounding zones, mitochondria show an increase in fusion. The researchers also succeeded in discovering a key metabolic process regulating astrocyte mitochondrial function: they were able to show that autophagy, a process involving the self-digestion of components in the cell, is critical to maintain mitochondrial structure. In contrast to neurons, astrocytes survive surprisingly well to acute inflammation. The new study reveals that autophagy is the major mechanism conferring this resistance. "When autophagy is ablated astrocytes loose their capability to regenerate their network which ultimately leads to their death", says Elisa Motori.

Although the reorganisation of metabolic pathways triggered by inflammation goes beyond the influence of mitochondria, these research findings clearly demonstrate that mitochondrial function is absolutely essential to astrocyte survival. Additionally they provide new insights for our understanding of how brain cells react to inflammation. Further characterization of these metabolic pathways may hopefully enable the researchers to protect neurons from dying during acute or chronic

neuroinflammation. This will potentially allow for the development of new approaches aimed at helping patients exposed to brain injury or stroke, in order to preserve brain function and improving the patient´s quality of life.

More information: "Inflammation-Induced Alteration of Astrocyte Mitochondrial Dynamics Requires Autophagy for Mitochondrial Network Maintenance." Elisa Motori, Julien Puyal, Nicolas Toni, Alexander Ghanem, Cristina Angeloni, Marco Malaguti, Giorgio Cantelli-Forti, Benedikt Berninger, Karl-Klaus Conzelmann, Magdalena Götz, Konstanze F. Winklhofer, Silvana Hrelia, Matteo Bergami. *Cell Metabolism* 2013. DOI: 10.1016/j.cmet.2013.11.005

Provided by Ludwig Maximilian University of Munich