Astrocytes and the Important Role in the Future Research of Brain

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Abbreviations: AD: Alzheimer’s Disease; Aβ: Amyloid β; PPAR-γ: Peroxisome Proliferator Activated Receptor γ; TFAM: Mitochondrial Transcription Factor A; PGC-1: Peroxisome proliferator-activated receptor γ Coactivator 1

Amyloid β (Aβ) deposition has been proposed as the major pathogenic event in the development and progression of Alzheimer’s disease (AD) [1,2]. There is strong evidence showing that Aβ deposition causes oxidative stress and inflammation as well as mitochondrial dysfunction [3-6]. Many cells are detected inside our brain, such as astrocytes, neurons, microglia and oligodendroglia. The community of researchers was studying the role of neurons for decades because of its important interventions in cell communication in the nervous system. However the other brain cells have been poorly studied as compared to neurons. Astrocytes are more abundant than neurons in brain and in fact, they are about 30 times more abundant than neurons. Also when research community studied Einstein’s brain, they noticed 3 times more astrocytes in Albert Einstein’s brain than in normal people. So many scientists are thinking about the important role of astrocytes in memory, inflammation, oxidative stress, etc. Which roles of astrocytes are inside the brain and what role it has in neurodegeneration and illness?

Results from Valles et al. and others demonstrate that Aβ1-42 induces apoptotic cell death in neurons [5]. Furthermore, astrocytes protect neurons against Aβ1-42-induced toxicity. In vitro and in vivo studies indicate that Aβ enters the mitochondria, promote an increase in reactive oxygen species, disrupts the electron-transport chain, and inhibits generation of ATP [6,7]. Deficient mitochondrial respiratory chain function may have catastrophic consequences for the long-term health and survival of cells associated with AD [8]. Moreover extracellular Aβ fragments, likely by inducing oxidative stress, have been shown to cause damage to mitochondrial DNA (mtDNA) [9,10] and are highly susceptible to oxidative damage [10]. Many proteins help astrocytes to reduce oxidative stress and inflammation. Mitochondrial transcription factor A (TFAM), is involved in mtDNA maintenance, including nucleotide formation, mtDNA stabilization and transcription [11]. Recent studies indicated that TFAM and PGC-1 over-expression may inhibit mitochondrial ROS generation and improve mitochondrial respiratory function [12,13]. Furthermore over-expression of TFAM has been shown to protect mitochondria against Aβ-induced oxidative damage in neurons [14].

Both oxidative damage and inflammation are elevated in brains from AD patients [15], but their pathogenic significance remains unclear. Central nervous system has its own resident immune system, in which glial cells not only serve the supportive and nutritive roles for neurons cells, but also engage in several inflammatory processes that defend the central nervous system from pathogens and help it to recover from stress and injury [16,17]. Normal glial functions can sometimes result in a serious and chronic neuroinflammatory cycle that actually promotes neurodegenerative diseases, constituting a viable target for the discovery or development of neurodegenerative diseases, such as AD [18-20]. Also astrocytes perhaps act protecting neurons in the mixer culture from the toxic action and this point of view needs more research investigation. Perhaps astrocytes protect neurons by an increase in mitochondriogenesis thereby obtaining a better processing of oxidative stress and an efficient inflammation control. The importance of glial cell-propagated inflammation disorders such as AD has been seen as a bystander effect, or epiphenomenon, occurring when damaged neurons develop an activation response by glial cells. Wyss-Coray et al. demonstrated a phagocytosis process by astrocytes to eliminate and destroy Aβ peptide plates [17] and Valles et al. [6] also showed anti-inflammatory effects after Aβ- induction in astrocytes.

In schizophrenia, for example, research community has discovered the relationship between immunologic genes and schizophrenia. So our point of view has changed and we think now that astrocytes and microglia probably play an important role in the development of that illness. They are realist and now are looking to diminish the action of those immunologic genes. Perhaps they need to replant all the medication giving to patients. Astrocytes will be in the next frontier.

TFAM in astrocytes might have multiple roles in protecting mtDNA against the toxic peptide. First, as a member of the high-mobility group of protein, TFAM could cover the entire region of mtDNA to form the nucleoid structure, protecting mtDNA from oxidative or inflammation modifications [11,13]. Second, TFAM could maintain mtDNA copy number by binding mtDNA in the form of the nucleoid structure [21]. Moreover, TFAM could initiate mtDNA transcription to induce mitochondrial biogenesis, which might effectively compensate the mitochondrial dysfunction [22] explaining mitochondrial DNA instability and metabolic shift in human cancer [23]. Another point of view in recent works indicates that SIRT-1 influences growth-factor responses and maintenance of stem cells and also appears to influence lineage cell-fate decisions of stem cells via redox status [24]. The possible return to a quiescent phenotype and demonstration the affectation of astrocytes to the amyloid peptide action is another part to be study by the research community. In the healthy brain, astrocytes provide essential services for brain homeostasis and neuronal function [25] and also astrocytes remove the toxic peptide when they are reactive astrocytes, prepared to attack virus and microorganisms. Why only research people only looking for neuron works? Why don’t we investigate the role of astrocytes in brain? Many people are thinking about that, let's see the future of research brain.

References

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Received December 03, 2012; Accepted December 08, 2012; Published December 26, 2012


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