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Astrocytes: Puzzle in Neurodegeneration

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Editorial

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ABSTRACT

Understanding brain complexity and occurrence of brain diseases is still a challenge for researchers worldwide. Despite of extensive research in this area the pathology of brain diseases is still enigmatic and incites us to further explore the disease initiation, progression and manifestation of degenerative mechanisms. Studies from last two decades have shown the potential and functional involvement of astrocytes in brain disease pathology but still their explicit roles are not known and need to be explored further in detail.

ASTROCYTES: PUZZLE IN NEURODEGENERATION

Understanding brain complexity and occurrence of brain diseases is still a challenge for researchers. Despite of extensive research in this area the pathology of brain diseases is still enigmatic and incites us to further explore the disease initiation, progression and manifestation of degenerative mechanisms. To date research findings have implied that most of the brain disease pathologies involve the analogous cell death mechanisms except the decreased level of specific neurotransmitters. The decreased level of neurotransmitter occurs due to loss of specific neuronal population which is well explored for the particular brain disease. However, the role of non-neuronal cells, which constitute approximately ninety percent of brain cells population, is still underappreciated in occurrence of disease initiation and progression. The neuroscientists are still inquisitive to comprehend their explicit and dynamic role in brain disease pathology. There are two kinds of hypotheses and believers are working in this research area. One scientific group is not accepting the functional role of the non-neuronal cells in brain disease pathology whereas the other group has shown and further exploring the role of such foremost non-neuronal population in brain disease pathology. Such controversial outlook of neuroscientist worldwide is might be due to several gaps and limited knowledge regarding their function and interaction with neuronal cells in brain. Previously the non-neuronal cells were considered as only supporting cells in brain anatomy. However, studies of last two decade have suggested their functional role in neuropathology [1-6]. Among non-neuronal cells the astrocytes and microglia are the most studied cells. In this article we are addressing the astrocytes related issue but other non-neuronal cells have their own vibrant involvement in brain disease and must be studied further.

Research in various areas of science like biophysics and biology has provided us the modern technologies like imaging for the identification of brain disease occurrence. But still the diagnosis of brain diseases at early phase is challenge for medical doctors. To date we are unable to find out any diagnostic marker for the brain diseases therefore, the patients went to the doctor when the conditions are already out of control. Due to no known prescribe biomarker doctors have to depend on imaging based diagnosis and certain classical psychological test, by which they could predict the disease up to some extent for appropriate medication and make the life better of brain disease patients. Further extensive research is required to identify the blood biomarker for the brain diseases. USA government has initiated number of research oriented programs for the identification of diagnostic markers for brain diseases (WHO 2006, Michael J Fox Foundation etc.) but in developing countries such program need to be initiated. In developed countries, the government has established national policies and programs whereas in developing countries the public is rarely aware about brain disease symptoms and occurrence due to various issues. The unavailability of diagnostic markers and delayed identification of disease cause the disease-worsening and makes the patient's and their family life tough both emotionally and financially. Like for dementia and Parkinson's related patients, full time caretaker which causes extra financial burden on

family. In developing countries the expenses for brain diseases is also one of the issues to remain unaware for these diseases till at their worst phase. Alone in United States the approximate expenses for the non-communicable expenses are more than 4000 million USD [7].

I would also like to grab the reader's attention towards the other issue which is related to the source of the information generated for understanding the brain disease mechanisms. Our most of the knowledge for the disease mechanism, by which we discover the new drug molecules, are actually from the animal data. This concern has numbers of limitations for the researchers including the anatomical restriction of brain, complex physiology and other ethical issues. Numbers of animal models are being used for exploration of disease mechanisms including transgenic and non-transgenic [8-10]. Non-transgenic animals models are usually include the administration of specific neurotoxins like for PD modeling the rotenone, 6-hydroxydopamine and lipopolysacchrides are mainly used [11-13]. For memory impairment the streptozotocin, scopolamine and okadic acid are being used [14-17]. Similarly for other diseases also specific neurotoxin has to be injected in specific area of brain or organ to mimic the neuronal loss as observed in patients of brain diseases [18]. The reason for using diverse neurotoxins for single disease is due to inability of neurotoxins to mimic the complexity of brain disease. We do not have any single neurotoxin which can mimic the complex biochemical and behavioral alterations of disease in animals. Due to such limitations we have to relate the animal findings with clinical findings and same are well accepted world widely. However, the effects of such neurotoxins on non-neuronal cells (which comprise the major population) remain neglected. Recently we have reported that rotenone induces the neuronal death in different brain regions and at the same time it involves the activation of astrocytes [17].

We have also assessed the effect of rotenone on specific astrocyte population and found that rotenone also exerts the similar kind of death as observed in neuronal cells [17,18]. Reports have suggested the involvement of oxidative stress, mitochondrial impairment, endoplasmic reticulum stress, protein aggregation, calcium homeostasis and apoptosis in most of the brain disease mechanisms [19-28]. Oxidative stress includes the inability of neurons to neutralize the overproduced reactive oxygen species, for which neurons are heavily dependent on their coupling with astrocytes [29]. The glutathione which is the real indicator of oxidative stress is maintained in neuronal cells with their close interaction with astrocytes. Also to maintain the physiological level of antioxidant enzymes like glutathione reductase and glutathione peroxidase, the neurons are closely coupled with astrocytes [30-33]. In one of our undergoing project we are evaluating the antioxidant property of astrocytes with aging. Findings have showed that decreased level of glutathione reductase in astrocytes in aged rats (unpublished data). We have also shown that astrocytes are also get affected with neuroprotectants suggesting that both neuronal and non-neuronal cells are important in brain pathology as well as during medications. To date various studies have shown the imperative role of astrocytes in brain diseases but still these cells are mysterious for the neuroscientists and need to explore in detail [33-38].

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