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Astrocytes: emerging role in immunomodulation and therapeutics an inclusive review

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Abstract : The brain contains certain key elements that aid in the processing of information. These astrocytes can modulate the activity at the synapse by altering the extracellular space volume, ion and neurotransmitter homeostasis. They also provide structural as well as metabolic support and regulate brain wiring and neurogenesis. Astrocytes in the human brain are much different from their rodent counterparts. The dysfunctioning of the astrocytes in the brain plays an important part in neuronal dysfunction which contributes in the pathogenesis in various disorders of the brain. On the contrary if we are able to alter the astrocyte dysfunction and target them for the therapy of brain diseases to bring about novel and effective approaches in time. The chronic pain pathogenesis take into account a number of cellular interactions between neuron like CNS-resident cells, microglia and astrocytes. Following the damages in the peripheral tissue, the astrocytes in the spinal cord transit to reactive conditions as well as have an active part in the mechanisms behind the nerve instilled pain. Studies have been done to prevent inflammatory-reactive activity of astrocyte and to restore inflammatory deregulation cellular changes. Astrocytes are now to show either strong pro-inflammatory action or crucial anti-inflammatory protective functions that are regulated by certain signaling inputs. The objective of this study is to summarize the different works that have been done in the last 15 years on astrocytes to bring about their role in immunomodulation and immunotherapy of various neuronal diseases like Alzheimer's disease, Down's syndrome, Stroke and the like.

Keywords: Astrocytes, immunomodulation, therapeutics.

Introduction

Astrocytes, the brain cells are found in the Central Nervous System, in the white matter and grey matter. Morphologically, there are two different astrocytes found, they are the protoplasmic and the fibrous astrocytes. While the protoplasmic is present in the grey matter and shows fine branching and is distributed densely around the cell body, the fibrous type of astrocytes are mostly localized around the myelinated fibres in the white matter of the brain and are characterized fibrous processes which are lengthy. The glial fibrillary acid protein (GFAP) filament acts as an astrocyte marker, though its expression in certain mature astrocytes might limit the *in vivo* use[1,2]. A specialized network of dense and finely branched feet-like processes extend from the body of the cells and aids astrocytes to connect to the neuronal synapses and cerebral blood vessels whose prime functionality are particularly regulated by the astrocytes themselves. Due to the judicious placement of these extending process-like structures and the biochemical and structural aspects of astrocytes, the cells are

optimized in their performance by the natural selection to perceive and respond dynamically to the different alterations in the microenvironment of the CNS.Due to some specialized molecular arrangement at the astrocyte-neuron junction, the astrocytes provide energy to the neurons and also control the metabolism of neurotransmitter, hence regulating their activity. They also regulate the homeostasis of synaptic transmission. The endfeet of astrocytes also help in the maintenance ad formation of Blood Brain Barrier (BBB) by projecting towards blood vessels, there they control the exchange of water and solute between the neural network and blood circulation. On the other hand, by connecting to the ependymal layer that borders the ventricles and the pial membrane, represent main neural interface with the external environment. Furthermore, with the help of certain specific communicating structures that is intercellular in nature, the gap junctions. Astrocytes are connected functionally and structurally with a much arranged and highly complicated network which allows them to coordinate the cellular activities, such as cell syncytium. This is done by the transfer of small ions and secondary messengers. Astrocytes are also capable of regulating the activity of adjoining cells, like neurons and oligo-dendrocytes, for long distances by communicating through the gap junction. The essential role of astrocytes is to maintain tissue homeostasis, they not only carry out main functions in the healthy CNS but are also involved in almost all pathological processes. Astrocytes activate complex biochemical processes and go through morphological changes, together known as "reactive astrogliosis" in order respond to a number of pathological insults, which might eventually lead to proliferation of cell and formation of scar. There is increasing evidence that alterations in astrocyte functionality play a crucial role in neurodegenerative diseases, metabolic diseases, inflammatory demyelinating diseases, intoxication, infections, leukodystrophies, migraine epilepsy, and schizophrenia[2].Moreover astrocytes have a role to play in the antioxidant immunomodualtory function. A number of pathological disturbances caused by astrocytes in due to the disturbance it causes in the myelin. Primary defect in the astrocyte causes disease in which myelin degeneration occurs.

Physiological role of Astrocytes in CNS

Evidences collected in the past few decades have brought into light that at several levels astrocytes are mostly involved in the maintenance of CNS homeostasis. On the other hand, in the molecular level they check the complete CNS by regulating the concentration and exchange of water, ions, neurohormones, neurotransmitters, metabolic substrates and energy. Astrocytes also control the organ and cellular homeostasis, being involved in synaptogenesis and neurogenesis as well as in the maintenance and formation of the BBB. These basic activities are directly related to specialized plasma membrane that are distributed in a polarized manner along astrocyte processes and are ready with specific macromolecular complexes and proteins that enable the astrocytes to exert different functions depending on which environment they are in.

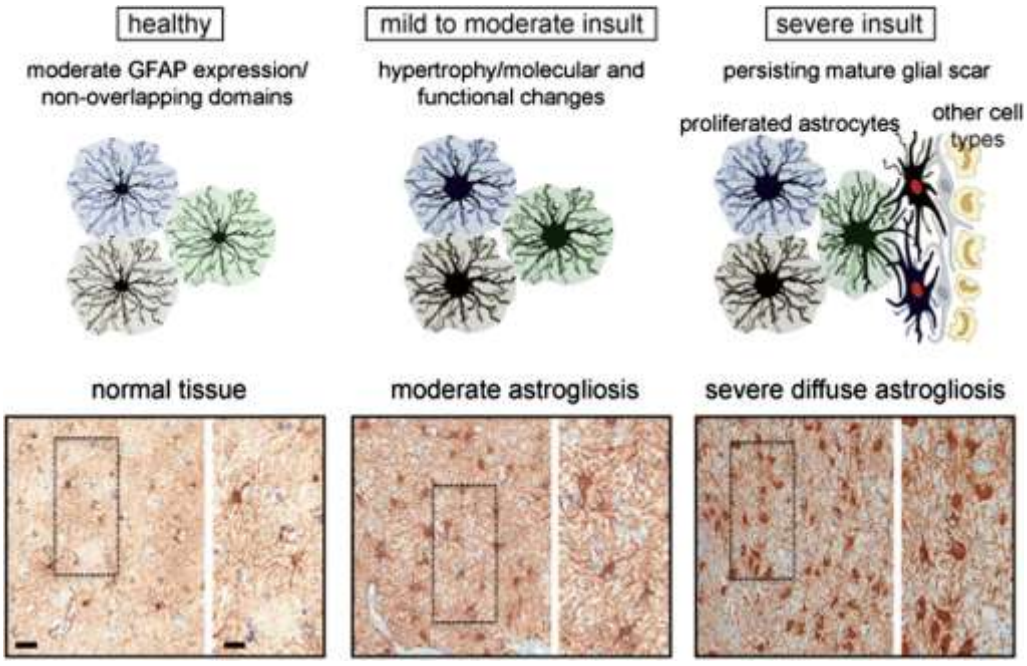

Fig.1 Human Brain Astrogliosis. Top, image represents the different grades of astrogliosis depending on the amount of the insult. Bottom, astrocytemorphology in normal tissue from a human specimen without lesion[3].

Relationship of Astrocytes with Neurons

Astrocyte-neuron relationships begin simultaneously with the development where astrocyte regulates neurogenesis by supporting and guiding neuronal migration, process extension and survival[4]. By releasing some trophic factors include brain-derived neurotrophic factor (BDNF), glial cell derived neurotropic factor (GDNF),nerve growth factor (NGF) , insulin-like growth factor (IGF) and thrombospondin[5-8]astrocytes in the forming, maintaining and remodeling. Additional factors obtained from astrocytes like glutathione, cholesterol, hydrogen sulfide and apolipoprotein E, is known to control neuronal function along with differences in *in vitro* and *in vivo* models[9]. An estimation has been made which shows that in the cerebral cortex and hippocampus a single astrocyte contacts about 100.000 or even more synapses which establishes a very regulated, two-way communication[10,11]. The uptake of the glutamate neurotransmitter is a prominent function of mature protoplasmic astrocytes. Amino acid, L-glutamate shows excitatory activity in CNS and its astrocyte clearance is as a result of the glutamate transporters: (EAAT1)excitatory amino acid transporter 1 and particularly EAAT2 and (GLAST) glutamate aspartate transporter and glial glutamate transporter 1 (GLT1)[12,13]. Astrocytes are known to activate ionotropic and metabotropic glutamate receptors which in turn cause Ca^{2+} influx[17]. Even though both astrocytes and neurons possess glutamate transporter, the entry of glutamate is essential for removing the excited neurotransmitter from the synaptic cleft. It is seen in the *in vitro* and *in vivo* experiments that this is the cause for 90% glutamate uptake[12.14]. After astrocytes take up the glutamate, it is mediated by a specific enzyme called glutamine synthetase which leads to neuronal nonreactive glutamine. This is then released in the extracellular spaces and serves as fuel for the neuron and via the glutamate-glutamine cycle is reconverted into glutamate[15,16]. The take up of other active neuro-tansmitters such as GABA, dopamine, norepinephrine, acetylcholine, glycine andserotonin[20] through the specified transporters that are shown at higher levels in the endfeet of astrocytes that contact the synapse[11,18,19].

Astrocytes and their connection with the blood brain barrier

Both fibrous and protoplasmic astrocytes establish a two-way process with the components of BBB [21]. The BBB hinders the entry of a number of molecules and the blood cells in the brain parenchyma, which in turn maintains the specific microenvironment need for proper functioning of the brain. The BBB forms tight junctions is said to be surrounded by pericytes, astrocyte endfeet and basal lamina on the abluminal side[22].Pericapillary end feet of astrocyte controlsthe inflow of nutrients, such as amino acids and glucose, from the circulation of blood along with certain transporters, and outflow of waste metabolites [23]. These endfeet are rich in the aquaporin 4 (AQP4) water channel which are membrane bound by the protein complex associated with dystrophin and cooperates with Kir4.1 to regulate K^+ and water exchange at the sites[24-26].Various ion channels aiding in the maintenance of cell volume[27-29], such as chloride channel ClC2, the putative ion channel MLC1 and the calcium channel transient receptor potential vanilloid-4 cation channel (TRPV4) are rich in astrocyte end feet contacting blood vessels to pial membrane[27,30,31].Experiments prove that interaction of astrocytes and astrocyte-derived factors such as growth factors, peptides, chemokines, cytokines, neurotransmitters and lipid substances, are vital for the maintenance and development of properties of BBB[32,33]. In cell culture, endothelial cells influence differentiation and growth of astrocytes[34].Astrocytes have localized blood flow in the Central Nervous System via substances such as prostaglandins (PG), arachidonic acid (AA) and nitric oxide (NO) that regulate blood flow and diameter of vessels in an orderly nature[35,36]. Astrocytes indeed control blood flow and vasodilatation as a response to the electrical activity hence the metabolism in neurons is supported with the help of brain tissue perfusion[37,38] by the process called functional hyperemia. Ca^{2+} signals travelling around astrocytic end processes activates the production of vasoactive substances which lead to the relaxation, and sometimes smooth muscles contraction, of parenchymal arterioles[39].

Astrocyte syncytium with astrocytes

Astrocytes connect to the nearby astrocytes with the help of gap junctions (GJ), that are made up of closely packed hemichannels named connexins aligned between adjoining cells[40].GJ mediates adhesion of cells to cells and helps in communicating and coordinating of contacting the cells through the cytoplasm passage directly and ion exchange, and small molecules such as second messengers and neurotransmitters[41].In glial cells of the CNS it expresses the biggest level of connexins (connexins 30 and 43 that represents the most important astrocyte specific connexins), Gap Junction channels and hemichannels[41].Astrocytesarrangement generate a multi-cellular functional and structural network that os considered as syncytium, important for physiological

functions as well as play a role in disorders of CNS[42].By astrocyte networks are known to spread K^+ ion along with glutamate quickly from synapses to blood circulation or other parts of the brain, and avoid their accumulation which can cause harm[43].Movement of Ca^{2+} ions between adjoining astrocytes provide excitability to these cells and shows the main way by which the astrocytes perceive and send across information. Simultaneously along with the movement of Ca^{2+} ion waves many calcium-dependent routes and biochemical processes are active that shows consequences in functions for astrocytes as well as their nearby cells[44].

Then again the Ca^{2+} ion waves, mechanical and electrical stimulation of astrocytes in culture induces metabolic waves which is mediated by Ca^{2+} ion dependent production of glutamate that further triggers a Na^+ion wave is generated as a consequence of the activity of Na^+ ion dependent transporters of glutamate[44,45]. This signal propagation is dependent on the take up of glucose and depends on the astrocyte and glutamate transporters which show neuro-metabolic coupling between neuronal activity and glucose utptake[46]. The crucial role of the Na^+ and Ca^{2+} ions are shown by controlling the intracellular ion concentration by various transporters and ion channels available in the plasma membrane of astrocyte[47].

The brain pathology of astrocytes

Taking into account the important activity of astrocytes in maintaining homeostasis of the Central Nervous System, it can be said that a change in the astrocyte-mediated physiological processes may show considerable effect on CNS pathology. Experiments show that neuronal symptoms lead to the neuro-degeneration is due to astrocyte homeostatic failure[48].Astrocytes have a vital role in the occurrence of various nerve related diseases[49-66].Moreover, the mechanism which controls homeostasis of the brain may be toxic in nature in case of strong insults or during its abnormal stimulation[48].Expression of aquaporin in perivascular membranes of astrocytes is important in regulating the exchange of water in the brain and is one of the reasons for occurrence of edema caused during cerebral stroke [67].It is one of the prominent instances of astrocytes pathological effect functionally. This slow process of astrocyte astrogliosis may lead to permanent glial scars depending on the type of insult[20,48,68]. Regulation of astrocyte reactivity based on temporal and kind of insult plays a key role to limit the tissue damage[69] and these changes in activation of astrocyte may lead to dysfunction of neural as seen in stroke, trauma as well as in multiple sclerosis[20].

Reactive type of astrogliosis is known to show severe effects in different levels, like worsening of inflammation alongside cytokine production, the release of glutamate followed by reactive oxygen species (ROS), changes of the structure of BBB and its function via production of vascular endothelial growth factor (VEGF), or AQP4 over reactivity that leads to cytotoxic edema in trauma and stroke[20,67,70,71]. In the same way, appearance of glial scar is helpful in encapsulation of infections along with tissue necrosis, might be troublesome for repair of tissues[68]. Release of glutamates from the astrocytes are maintained by inflamed molecules, likePG[72] and tumor necrosis factor (TNF), suggesting that connection of neuron to glial signaling is hindered by response to inflammation. It is not alarming that the list of diseases of the CNS caused by astrocyte dysfunction and excessive reactivity play and pathologically important role and is being worked upon continuously[48]

Table 1.Astrocyte contribution to CNS pathology[*]. (Table adapted from Reference[73])

Astrocyte-Mediated Process	Molecules Involved	Pathological Effect	Disorder	References
Glutamate Homeostasis	EAAT1 (GLAST) EAAT2 (GLT1)	Excitotoxicity	Epilepsy, Trauma, Stroke, Alzheimer's Disease, Amyotrophic Lateral Sclerosis, Huntington's Disease	49-53
Calcium Signalling	AMPRS_** mGluRs	Inhibitory and Excitatory Activity on neurons	Migraine, Epilepsy	54

K^+ and Na^+ Homeostasis	Kir 4.1 and other Kir channels $Na^{+,}$ K^+-ATPase	Spreads Depression, Edema, Neuronal Hyperexcitability,	Stroke, Epilepsy, Migraine, Trauma, Autism, Cytotoxic edema	55-58
Water Homeostasis	Aquaporin-4	Edema	Trauma Ischemic edema Stroke	67,59,60
Cholesterol Production	Niemann-Pick disease, type, C1(NPC1)	Oxidative Stress Deposition of Cholesterol in Excess	Niemann-Pick Disease	61,62
Long-Range Signalling	Cx30 Cx43	Spreads apoptotic signals and death	Epilepsy, Stroke	42-63
Neuro-glial Signalling	GluR1-4, NR1,2,3, Purinergic P2 receptors ($P2X_{1/7}$)	Excitotoxicity,Ca^{2+}/Na^+ Overload	Neuro-degeneration, Stroke	47,64,65
Releasing Toxic Substances and Reactive Astrocytosis	Inflammatory and apoptotic mediators, Nitric Oxide reactive Oxygen species/SOD	Neurotoxicity	Parkinson's Disease, Alzheimer's disease, Amyotrophic lateral Sclerosis	50,52,66

*Infectious and tumoral diseases are not included in this table.

**α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid subtype glutamate receptors (AMPARs)

Multiple roles of astrocytes in regulating myelination

Hulya Kiray and his team said Astrocytes which are the glial cell of the Central Nervous System, provides metabolic as well asphysical aid to the different neural cells. Glial fibrillary acidic protein (GFAP) filaments were used on a large scale to study astrocytes More the GFAP expression the more is the astrocyte reactivity and hence the lesion in CNS is a sign for disease or injury. After an injury, the astrocytes show reactivity while expressinga phenotype that might show excitatory/inhibitory functions and in the repair of the CNS and its proper functioning.

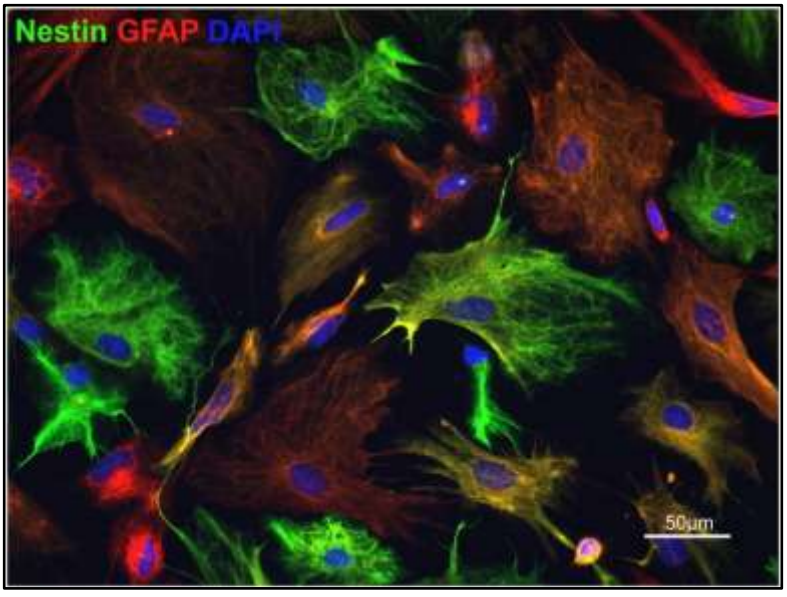

Fig.2.Expression of astrocyte reactivity markers[74].

Astrocytes influence the myelination in certain specified cases, neuronal cell targets and cytokines within the CNS.

Astrocytes are capable of influencing the myelination in terms of certain specific secreted factors, some neural cell targets and cytokines within the CNS. Astrocyte is also known to provide cholesterol and energy to all neurons and have an influence on synaptogenesis, affect oligo-dendrocyte biology[75] and initiate the cross-linking between various components present within the Central Nervous System. In an experiment allergic encephalomyelitis (EAE) which is a widely used animal model for MS, where myelin antigens to induce demyelinationis administered together along with substances that possess bacterial components[76]has been used to prove this. Thus the amount of GFAP immune-reactivity depicts the level of reactive astrogliosis.

Optogenetic Stimulation of Spinal Astrocytes and their relationship with Reversible induction of Pain Hypersensitivity

Youngpyo Nam *et. al*. showed experimentally that the glial activation is an important part of pain pathogenesis, the presence of a simple relationship between glia and pain processing is yet to be worked upon *in vivo*. Investigations have been undertaken to prove that the activation of spinal astrocytes may directly cause pain hypersensitivity in vivo via the use of optogenetic processes and techniques. The Optogenetic stimulation of channelrhodopsin-2 (ChR)- that express pain hypersensitivity induced by spinal astrocytes in a time dependent and reversible way, was accompanied by the activation of glial cells, ATP release,NR1 phosphorylation, and proalgesic mediator production. Excited astrocytes present in the spinal cord (in dorsal horn) aid in central sensitization by the release of ATP and neuromodulators such as cytokines, chemokines, and other growth factors[77].

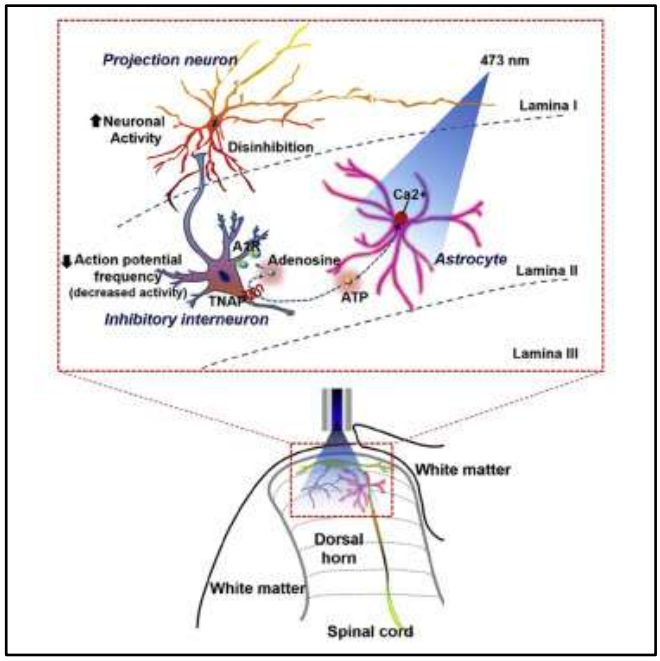

Fig 3. Pain Hypersensitivity(Reverse induction)[78]

Photostimulation of astrocytes expressing ChR2 in culture mediumand spinal slices recapitulate the *in viv o*data, demonstrating the production of proalgesic mediators along with electrophysiological disinhibition of spinal projection neurons. This portray the astrocytic role in pain pathogenesis[79] providing scientific understanding for an astrocyte-mediated pain treatment.

Astrocytes as targets of inflammation and Inflammatory-reactive activity

Elisabeth Hansson *et. al.* worked on pharmaceutical compounds that target the astrocytes and show their dysregulation. They used the primary brain cultures from rats and treated them with different serum batches which either contained microglia or was devoid of it. This made them inflammatory-reactive in nature. Lipopolysaccharide (LPS) and tryptase were used for inducing inflammation. Then the levels of expression for

receptors like 4 (TLR4), Na^+/K^+-ATPase, and matrix metalloprotease-13 (MMP-13) along with the organized actin filament, the release of intracellular $Ca^{2+}$and pro-inflammatory cytokines were taken into account and evaluated.

The LPS was seen to combine with the tryptase and increase the TLR4 expression on one hand, whereas on the other it decreased the expression of Na^+/K^+-ATPase, the actin filaments were reorganized in ring formations instead of stress fibers[80]. The astrocytes were prevented from their inflammatory reactive nature and their inflammatory dysregulated cellular changes were restored. The dysfunction of astrocyte may be caused due to genetic polymorphism or by exposing them to molecular signalling obtained by infectious trauma which may change the regulation of astrocyte inflammation and cause severe effects. At tissue damage sites, the astrocytes form scar border by becoming reactive in nature. This in turn, serves as functional hindrance and is capable of releasing molecules that have the tendency to affect the cells nearby[81]. The MMP-13 produced by neurons and astrocytes increase the inflammation response in the brain and remodels the extracellular matrix, thereby degrading the substrates as a part of neuro-inflammatory response[82].

Functional Astrocytes Created with Small-Molecule-Based Lineage Reprogramming

E.Tian *et. al*. Pin-pointed at the growing evidence which indicated the key roles of astrocytes in neurodevelopment and diseased state. According to them, the recent progress in the reprogramming the somatic cells as various neural cells, reprogramming to astrocytes is not quick. They have shown how the functional astrocytes have been generated using small molecules from the fibroblasts of mammals. Mouse astrocytes can resemble primary astrocytic gene expression and epigenomic status, exhibiting the functional properties to promote the neuronal maturation along with calcium signaling and glutamate uptake. These induced cells can imitate the phenotype of aggregated protein in case of Alexander's disease while expression the GFAP with mutations that are capable of causing diseases[83]. Chemically induced astrocytes can provide cellular models that will reveal the role of astrocytes in normal neurodevelopment as well as in the pathogenesis of neurological diseases.

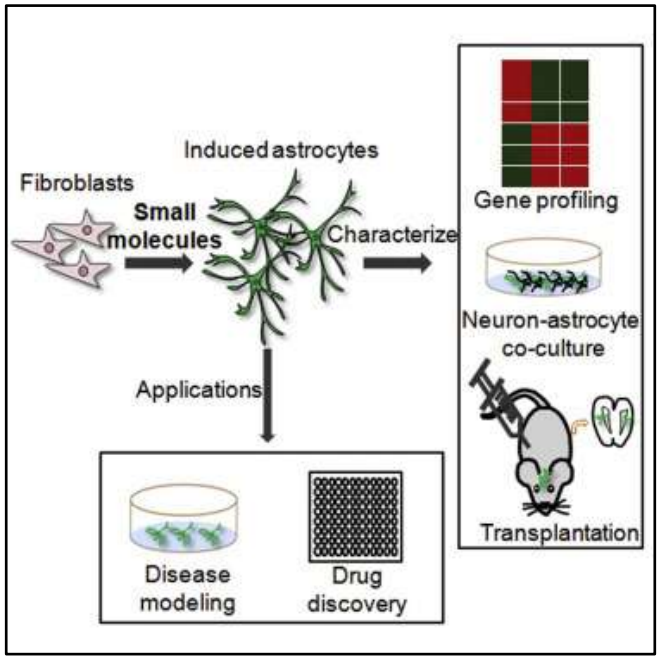

Fig 4. Lineage Reprogramming creating functional astrocytes[83]

The knock-down of the glutamate transporter, GLT-1 influences the differentiation of neural stem cells as an effect of astrocytes

Release of major levels of glutamate during neurotransmission is taken up by the GLT-1 glial transporter into the astrocytes; the extracellular glutamate is inactivated by this process. The study by Yijing Guo and his team determined that to what level did GLT-1 mediate the regulation in astrocytes of the cell fate

of neural stem/progenitor cells (NSCs) by reuptake of glutamate. Faijerson *et al.* modeled astrogliosis *in vitro* using mechanical lesions of primary astrocytes. It was found that the astrocyte lesions stimulated the astrocyte differentiation of NSCs without showing much effect on the oligo-dendrocytic or neuronal differentiation[84].NSC and astrocyte co-culture increased the synaptophysin protein levels of NSC-derived new neurons through GLT-1[85].

Iron uptake by astrocytes activated by inflammation showing regulation of iron burden in neuroprotection

Astrocytes play a very important role in the handling of iron in the CNS. This is a fundamental function during neuroinflammation and during any neurodegenerative process where the iron increase can favor oxidative stress which makes the progression of the disease worse. Under certain pathological situations, these astrocytes go through an activation process that renders it as a threat or benefit to the survival of the neuron. The data obtained from various experiments suggest that the non-transferrin-bound iron (NTBI) is the key iron producer and it shows involvement of two different entry routes, resident transient receptor potential (TRP) and the newly shown divalent metal transporter 1 (DMT1) available in quiescent and active astrocytes respectively. These two are the main components known to contribute to the entry of iron. Some data suggested that not only at rest but when activated as well, these astrocytes have the potential to prevent excess iron and thus protect neurons. These data show that the astrocytes play protective role in certain oxidative stress caused by iron and is a key observation in many neurodegenerative conditions[86.]

Neurons and astrocytes regulate the brain's antioxidant defenses

The brain is capable for homeostasis and the glial cells and the neurons have built-inprocess which help them in showing protective and adaptive response in challenging situations, that ensure that the variability and the functionality of the brain remains intact. There are many requirements of the brain and which include the work to neutralize the related reactive oxygen species (ROS) released which limits the damage in the brain. These astrocytes, as already known, provide antioxidant support to neurons aroud[87], redox regulation of the Nrf2 pathway of astrocytes is a potent homeostatic regulator. This pathway is not strong in most nerve cells and thus robs it of the homeostatic nature. These various homeostatic mechanisms in neurons and astrocytes together promote resistance of nerve cells from oxidative insults. Future experimentation into signalling between different cell types inside the neuro-glial unit which are known to uncover the other related mechanisms underlying the redox homeostasis occurring in the human brain.

Human astrocytes into stem cells and nerve cells: Reprogramming

Reprogramming of the human astrocytes is one of the useful strategies to repair of neurons. Experiments showed the dedifferentiating the the cortical astrocytes of the humans into neural stem phenotype which helps in obtaining the progenitor and mature neural cells. Ectopic expression of factors includes, SOX2 OCT4 or NANOG to astrocytes in certain culture of cytokine that activates the programming of genes in the neural stem cell. Pure CD44+ mature astrocyte show changes in lineage commitment and does not need to pass through pluripotent state[88]. These so called neural stem cells obtained from astrocytes gave rise to neurons and astrocytes along with oligo-dendrocytes. They revealed engraftment properties inside the model as well. Enhancing and restoring the multi-potency of astrocytes of humans show a possibility in cellular reprogramming in the CNS cells in case od neurological disorders.

Acute homeostatic response an sign for a functional astrocytic role in high fat intake in mice

Hyperphagia is a condition of voracious feeding in mice as a result of introduction of high-fat diet. Before the homeostatic mechanism restore energy intake in isocaloric level response. This condition induces the activation of astrocyte in rat hypothalamus. This in turn, proclaimed that cells play an important role in the homeostatic response to diet[89]. Studies have been done to determine the astrocytic role in homeostatic response in relation to high fat diet. For an experiment transgenic mouse were bred with NFkappaB which were inhibited by doxycycline-inducible signaling to show the sign of loss of NFkappaB-induce dactivation of astrocyte on acute high-fat diet in mice. ELISA technique was used to quantify the level of activation, GFAP and S100B in basal hypothalamus. This experiment in turn showed that inflammatory signaling of astrocyte is induced as a result of the high-fat-diet and it shows the protective response of the astrocytes to the homeostatic response. This in turn inhibits food intake by the experimental animal.

Conclusion

In a survey of 20 years, it has been seen that the astrocytes has a very crucial role to play in the human brain, the function and activity of astrocytes in human brain have been detected and defined over the years. It is determined that a number of neuronal diseases are associated with astrocyte dysfuntion. Due to the malfunctioning of astrocytes diseases like Alzheimer, Down's syndrome, Epilepsy, Stoke, Trauma etc. can be caused. Different studies above have proved the same. However controlling and inhibiting the malfunction of astrocytes and the glial brain cells and those present in the spinal cord may also prove to have certain beneficial effect on the curing of diseases. Various works are now focused on the same. Astrocytes are potential modes of therapeutics and immunomodulation for different prevalent neuronal diseases in the current scenario. Many methods have been incorporated by different groups of scientists and they followed different conclusion to prove the immune-modulatory and therapeutic effect of astrocytes. Studies have shown the by regulating the activity of astrocytes a number of neuronal diseases such as Parkinson's Disease, Alzheimer's Disease and the like can be treated. However the concrete pathways for the same are yet to be discovered. Scientists are now focusing on the individual studies of the astrocytes and the specified function in various diseases. In the years to come it is expected that some concrete results and methods for curing some of these deathliest neuronal diseases will come into the limelight.

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