Introduction

- The five types of glial cells that exist in the central nervous system (CNS) include Astrocytes, Oligodendrocytes, Microglia, Ependymal cells, and Radial glia.
- Astrocytes are the most numerous cells in the mammalian brain (cortical grey matter)
- The ratio of astrocytes to neurons in the whole human adult brain is 1:1 (Azevedo et al., 2009) and with a ratio of 1:4 in the cerebral cortex
- The morphology of astrocytes is best described as an interface between vascular and neuronal networks. The strategic positioning of astrocytes is well matched with the classically supposed functions of astrocytes, including the clearance of synaptically-released neurotransmitters (NTs), regulation of ionic concentrations and mediation of energy metabolism substrates
ASTROCYTES' TRANSPORTERS AND CHANNELS

- Astrocytes possess glutamate receptor and transporter
- Glucose transporter
- Calcium transporter
- Monocarboxylate transporters (MCTs),
- Kir4.1 a weakly inwardly rectifying K+ channel
- TREK-1 a glutamate release channel and TWIK-1 as a sensor of glutamatergic transmission
- Astrocyte connexin hemichannels shape basal synaptic transmission
- inositol-1,4,5-triphosphate (IP3)-dependent
FUNCTIONS OF ASTROCYTES

• Regulates glutamate
• Uptake and regulation
• Ion regulation
• Glycogen energy reserve
• Promote neuronal survival
• Blood brain barrier
• myelination
• immune modulation
• Modify Extracellular fluid
GLUCOSE TRANSPORT IN ASTROCYTES

• Glucose is transported across the cell membrane by two types of glucose transporters;
  ✓ sodium dependent glucose transporters (SGLTs)
  ✓ sodium independent glucose transporters (GLUTs)

• GLUT1 occurs in brain in two isoforms;

• The more glycosylated form and the less glycosylated form

• The less glycosylated form is localized in astrocytic end-feet and cell bodies. It is not present in axons, neuronal synapses or microglia.

• Glucose transported to astrocytes by GLUT1 and metabolized to lactate serving to neurons as energy source.
CALCIUM TRANSPORT IN ASTROCYTES

• Astrocytes exhibit a large number of G Protein-Coupled Receptors (GCPRs) linked to Ca2+ mobilization from internal stores.

• Astrocytes undergo elevations in intracellular calcium concentration following activation of G protein-coupled receptors by synaptically released neurotransmitters.

• Ca2+ waves in astrocytic network glutamate release by astrocytes.

• These receptors can be activated by neurotransmitters released from presynaptic terminals.
Agulhon et al., 2008
CALCIUM TRANSPORT IN ASTROCYTES

• During quiet wakefulness, the cortical noradrenergic and cholinergic pathways release low levels of neuromodulators, and astrocytes display transient asynchronous Ca2+ fluctuations within their processes.

• In active brain states, there is increased cortical noradrenaline (NE) and acetylcholine (ACh) release. This activates Gq-coupled receptors located on astrocytes

• Generating global astrocytic Ca2+ signalling.

• The increase in Ca2+ level in astrocytes lead to increased uptake glutamate (Glu) from the extracellular space into astrocytes thereby possibly regulating the excitability of neural circuits.
Glutamate is released during neuronal transmission into the synaptic cleft.

Astrocyte clear glutamate from the cleft through facilitated diffusion with aid of a carrier which cotransport one glutamate along with three sodium ions.

Thus intracellular sodium ion concentration increases after sodium uptake.

This activates Na/kATPase, leading to increased energy demand by the astrocytes after neuronal discharge.

This leads to energy demand and consequently lactate release.

The lactate is released and taken up by the neurons as substrate.
Astrocytic Glycogenolysis, Aerobic Glycolysis, and Lactate Are Critical for Long-Term Memory

• Glutamate release, stimulates the uptake of glutamate by astrocytes, which is converted into glutamine (glutamate–glutamine cycle), which sustains synaptic release of glutamate.

• This cycle requires energy from astrocytes, which would therefore activate glucose uptake from the blood and metabolize it into lactate.

• Lactate, released by astrocytes via monocarboxylate transporters (MCTs), enters other types of cells using similar transporters, which operate on the basis of concentration gradients of protons and monocarboxylate across the plasma membrane
POTASSIUM TRANSPORT IN ASTROCYTES

- Due to different combinations of and subunits isoforms of NaKATases in neurons and astrocytes, their kinetic characteristics and binding affinity are different, allowing astrocytes to respond faster to the immediate release of K+.

- During normal brain activity, the astrocytic NaKATases temporarily pump out the residual K+ ions leading to decreased [K+] and neuronal hyperpolarization.

- Leading to extracellular increases in [K+],

- Na+-K+-2Cl− cotransporter (NKCC) utilizes the Na+ electrochemical gradient to transfer Cl−, K+ and Na+ ions along with water influx through the membrane, thereby resulting in overall astrocytic swelling.

- Cellular swelling has been used as a marker of astrocytic net K+ uptake.
POTASSIUM TRANSPORT IN ASTROCYTES

- Astrocytes, the prevailing subtype of glia in the cortex, are highly connected and can modulate the excitability of neurons by changing the concentration of potassium ions in the extracellular environment, a process called K+ clearance.

- The mechanisms involve both voltage-dependent and transport-mediated ion fluxes combined with intercellular communication via gap junctions.
References


