Astrocyte – Neuron Cross Talk

Arun Chaudhury Anatomy, AIIMS

Neuroglia (Kitt)



Rudolf Virchow

Ramon Cajal



Camillo Golgi



Astrocytes – form & distribution

Fibrous astrocyte

Very long thread like

process

GFAP +



Surface of brain, spinal cord, white matter, hippocampus, ant./ dorsal horn of sp. Cord except substantia gelatinosa **Protoplasmic astrocyte**

Short sinuous process with cluster of lamellar appendages of grey matter Astrocytes – form & distribution

Special forms

Radial glia

Bergmann glia

Muller cells (GFAP + after injury in rats,

+ve in goldfish)

tanycytes

Pituicytes
GFAP +
Posterior pituitary
Interstitial cells of
pineal

Neuronal Migration & Glia

Radial glial cells in developing brain

Vimentin, GFAP, S100



Specific cues for axonal trajectories provided by glial cells lessons from retinotectal pathway



Glucose requirement in brain

Indispensible

Logistic challenge

Glucose metabolism in neuronal cells & astrocytes



Glia as carbon dioxide sinks



Glutamate receptors **Ionotropic receptors** (ligand gated ion channels) Alternative splicing AMPA **Kainate** (DRG, Hippocampus) **NMDA** (Muller Cells, Visual cortex, Bergmann glia)

Ionotropic receptors



Glutamate receptors

Metabotropic receptors

Gs / Gi

IP3 ----- Ca++

Ca fluctuation – role in circadian rhythm

Tripartite synapse – glia, the unclaimed partner



Metabolic trafficking between astrocytes and neurons



Structural neuron – glia plasticity **Parturition** Lactation **Osmotic stimulation** Astrocytic coverage of magnocellular neurons of SON/ PVN

Pituicyte contraction

Highly sialylated weakly adhesion isoform of PSA - NCAM

Glutamate receptor mediated signalling to nucleus

Activation of AMPA in Bergmann Glia Ca++ AP –1 (activator protein) IEG activation (c-fos, c-jun c-myc, NGPI – A)

Neurovascular coupling



Glial Cells



Glial limiting membrane

continuous lining separating brain from mesenchymal structures with intervening basal lamina

Blood Brain Barrier

Insects – glial cells

Sharks, skates, rays – open endothelial layer & tight junction between astrocyte end – feet & capillary

Human – tight endothelial junction with surveillance from end–feet of astrocyte



Astrocytes release neurotransmitters



Calcium metabolism in astrocyte

Are glial cells excitable cells?



Effect of intra-astrocytic calcium

Local calcium oscillation

Gap junction (dye coupling, freeze fracture)

(Cx 43, Cx30)

long distance signalling of calcium wave (GJIC)

Low resistance pathways

Increased cytosolic calcium implicated in hypoxia, hypoglycemia, HIV gp120

Glial membrane potential High permeability to K+ ions 20 mV more (-) RMP than neuron Glial cells hyperpolarise during onset of neuronal activity ? Inadequate number of Na+ channels Glia – neuron dialogue in chemosensitive brain areas - discharge I n response to pН

Potassium spatial buffering

High neuronal activity (mesencephalic reticular formation) [K+]e = 3.5 mV - 12 mVAstrocytes help in siphoning K+ from ECS No explosive voltage dependent conductance Slow potential shifts (SPS)



Is brain insulated from effects of immune system?

Brain grafts

BBB

Absence of lymphatics TGF β , neuropeptide, ganglioside – immune suppressor

Low expression of MHC

Apoptotic elimination of T cells

Th 1 vs. Th 2 response

Th 1 CD 4+ Th 1 APC IL-2, γ–IFN, TNF β

Th 2 IL -4, IL -10, IL-13 Downregulate Th 1 response

Microglia – Tissue guardians of brain

Ontogenically ~ mononuclear phagocyte lineage

? Neuroectodermal origin

- Resting microglia
- Activated microglia

Activated glia

Highly plastic Stereotypic activation Rod shaped (syphilitic paralysis) Nodules (spinal neiurons of anterior horn in poliomyelitis)

Foam laden macrophages

Gitter cells

Activated glia



Receptors on microglial cell surface





Microglia in CNS inflammation



T cell restimulation



Functions of microglia

 Professional phagocytes – ORF, NO, proteases

(microorganisms, debris)

- 2. Wound healing
- 2. Demyelinating diseases
- 3. ? Alzheimer's disease
- 4. Delayed hypersensitivity

Astrocyte in CNS inflammation

- PGE2, TGF β Th 2 response
 limit inflammation & support
 neuron survival
- IL 4 --- NGF
- MCP -1, IP- 10, RANTES

recruitment of cells



Gliosis vs. fibrosis

† GFAP expression by astrocytes in brain damage

IL – 1 β –> astrocyte mitosis if BBB disrupted

Scrapie –> IL –1 / TNF α – intense gliosis

Glial scar & epileptogenesis

Gliosis

- During fibrillogenesis, is uptake of glutamate inhibited?
- ECF excitotoxicity & penumbra in infarcted area
- Are the glial cells derived from site of injury or have they migrated?
- Can the glial cells secrete stromyelesin to digest brain versican?

Injury to brain

• MPTP----- \rightarrow MPP+ (Parkinson's disease)

• 3-HAO (in astrocyte) --- quinolinic acid

damages neurons in Huntington's disease

Brain edema in hepatic encephalopathy



Cirrhosis of liver

Reye's syndrome

Alzheimer's type II astrocytes (cerebral cortex, basal ganglia)

Role of astrocytes in regeneration in CNS

GDNF - regeneration of dopaminergic neurons

Olfactory glia – role in CNS regeneration

