

Hydrostatic Pressure Induced Activation of Sodium Hydrogen Exchanger in Optic Nerve Head Astrocytes: Role of Calcium

The plasma membrane Na^+/H^+ exchanger NHE1 has an established function in intracellular pH and cell volume homeostasis by catalyzing electroneutral influx of extracellular Na^+ and efflux of intracellular H^+ . Primary Open Angle Glaucoma (POAG), a progressive optic neuropathy, is characterized by intraocular pressure (IOP) greater than the normal (15 mmHg), is characterized by the loss of retinal ganglion cell's (RGC) axons and remodeling of the extracellular matrix (ECM), involving both the optic nerve head and the retina. In the eye, optic nerve head structure and RGC's well being is strongly influenced by the astrocytes. Astrocytes are essential for neuronal survival, play important roles and provide nutritional support to neurons by regulating its intracellular pH and ion balances. Elevated hydrostatic pressure (HP) (15 or 30 mmHg) for 2h causes phosphorylation of ERK1/2, ribosomal S6 kinase (p⁹⁰RSK) and NHE-1. The cultured astrocytes when challenged with elevated HP (15 mmHg) in a closed chamber and cytoplasmic calcium responses were measured, had shown an elevated HP induced immediate slow rise in cytoplasmic calcium $[\text{Ca}^{2+}]_i$. Ryanodine receptor (RyR) antagonists, ruthenium red (10 μM) or dantrolene (25 μM) inhibited the HP-induced calcium rise and the rise was abolished when ryanodine-sensitive calcium stores were pre-depleted with caffeine (3 mM). Calcium store release appears to be a required early step in the initial astrocytes' response to an HP increase and a trigger for eventual NHE activation.