OPEN ACCESS
ARVO Annual Meeting Abstract | July 2018

Expression and activation of SAPK/JNK in the ONH in a rat model of ocular hypertension

Teresa Mammone; Glyn Chidlow; Robert J Casson; John PM Wood

+ Author Affiliations & Notes

Investigative Ophthalmology & Visual Science July 2018, Vol.59, 6069. doi:

Abstract

Purpose : Stress activated protein kinases (SAPK/JNK) constitute a sub-group of the mitogen activated protein kinase family. SAPK/JNKs are involved in neuronal microtubular stability and axon transport and are also known to play key roles in cell death and survival in a variety of retinal damage models. They therefore likely contribute to retinal ganglion cell (RGC) death in diseases such as glaucoma. We investigated SAPK/JNK activation, via changes in phosphorylation status, in a rat model of increased intraocular pressure (IOP), in order to provide further information as to the role of this enzyme group in glaucomatous RGC loss.

Methods : An experimental rat model of chronic ocular hypertension (OHT) was established by laser-induced coagulation of the trabecular meshwork. SAPK/JNKs, as a whole, were subsequently investigated over the following 14 days for expression and activity changes, using real-time RT-PCR, immunohistochemistry and Western immunoblot.

Results : Total SAPK/JNK expression was unaltered in control and treated eyes after IOP elevation. SAPK/JNK was present in all samples and was unaffected by chronic OHT when analysed by real-time RT-PCR, immunohistochemistry and Western immunoblot. Activated SAPK/JNK was present in untreated eyes, localising in RGC axons in the retina, optic nerve head (ONH) and optic nerve. However, after IOP elevation for 3 hours, phosphorylated SAPK/JNK (p-SAPK/JNK) was significantly elevated in ONH extracts. Immunohistochemistry also revealed that p-SAPK/JNK labelling was no longer evenly distributed throughout axons but had accumulated within the ONH region relative to the optic nerve after 6 hours of raised IOP.

Conclusions : Total SAPK/JNK and activated p-SAPK/JNK are present in the retina, ONH and optic nerve in untreated retinas. However, elevation of IOP causes activated SAPK/JNK, which is present throughout RGC axons, to quickly accumulate at the ONH. Although p-SAPK/JNK has been detected in optic nerve extracts from control eyes, it has not previously been localised to RGC axons. Activation of SAPK/JNK in the retina, ONH and optic nerve as a result of IOP elevation suggests that this enzyme group could play a role in the developing pathology in our model, and, by implication, in the pathogenesis of glaucomatous RGC loss.

This is an abstract that was submitted for the 2018 ARVO Annual Meeting, held in Honolulu, Hawaii, April 29 - May 3, 2018.