Shahnawaz Ali Bhat et al., J Alzheimers Dis Parkinsonism 2016, 6:5(Suppl)
http://dx.doi.org/10.4172/2161-0460.C1.021

Platelet CD40L mediates activation of Astrocytes and Microglia culminating in Neuronal injury in brain regions associated with Memory functions during Chronic Hypertension

Shahnawaz Ali Bhat, Ruby Goel, Rakesh Shukla and **Kashif Hanif**
CSIR-Central Drug Research Institute, India

Studies have reported hypertension as a prominent risk factor for dementia. Further, earlier reports have separately demonstrated that chronic hypertension is associated with platelet activation in periphery (resulting in accumulation and localized inflammatory response) and glial activation in brain. We investigated the contribution of platelets in brain inflammation, particularly glial activation and associated neuronal injury *in vitro* and in a rat model of chronic hypertension. We found that chronic HTN increased the expression of adhesion molecules like JAM-1, ICAM-1 and VCAM-1 on brain endothelium and resulted in the deposition of platelets in brain. Platelet deposition in chronic hypertension was associated with the augmented CD40 and CD40L and activation of astrocytes (GFAP expression) and microglia (Iba-1 expression) and increased caspase 3 expression and more TUNEL positive cells in the brain. Platelets isolated from hypertensive rats had significantly higher sCD40L level and induced prominent glial activation than platelets from normotensive rats. Moreover, CD40L induced astrocyte and microglia activation and NFκB and MAPK inflammatory signaling, with subsequent release of inflammatory TNF-α. Remarkably, conditioned media from CD40L activated glia induced the apoptosis in neuronal cells, Neuro2A (evidenced by increased Annexin V/PI +ve cells via flowcytometry). On the contrary, inhibition of platelet activation by clopidogrel or disruption of CD40 signaling prevented astrocyte and microglial activation and provided neuroprotection in both *in vivo* and *in vitro* conditions. Thus, we have identified platelet CD40L as a key inflammatory molecule for the induction of astrocytes and microglia activation, the major contributors of inflammation mediated neurodegeneration in brain.

shahnawazalibhat@gmail.com

Notes: