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The CXCR4/CXCL12 axis contributes to cerebrolysin-induced neuroprotection against staurosporine-treated cortical neurons at 7 days in vitro and prevents inflammation in a N2a cell line exposed to LPS

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INTRODUCTION

Oxidative stress and inflammation are hallmarks of neurodegenerative diseases, including a reduced repair capacity. Neural progenitor cells (NPCs) from the subventricular zone (SVZ), the dentate gyrus and the olfactory bulb can migrate and differentiate into neurons or glial cells. CXCL12 chemokine binds to CXCR4 and this axis contributes to neuroinflammation.

Following CNS insult, chemokines recruit stem cells for repair while the aberrant CXCR4 activation promotes cell death. In fact, NPCs, endothelial cells, neurons (and glia) express CXCR4, which enhance the homing of stem cells for neuronal repair. CXCL12 attracts neuroblasts and it is also secreted at sites of injury.

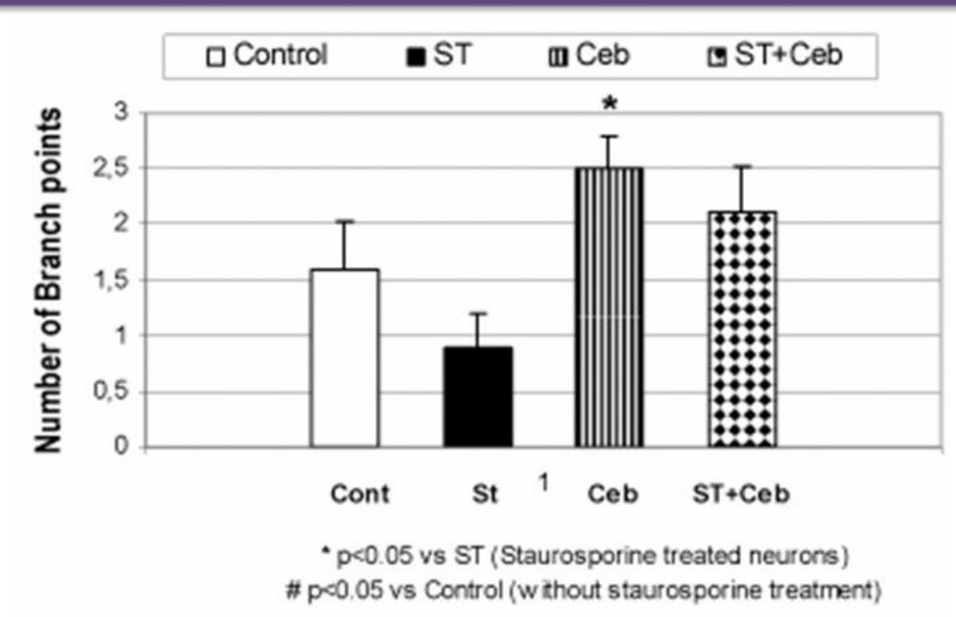
Neuroprotective effects of cerebrolysin

Cerebrolysin (Ceb) contains low-molecular weight neuropeptides from porcine brain proteins and induces neurotrophic BDNF-dependent levels. Ceb was approved for acute ischemic stroke, cognitive impairment and dementia treatment (USA)

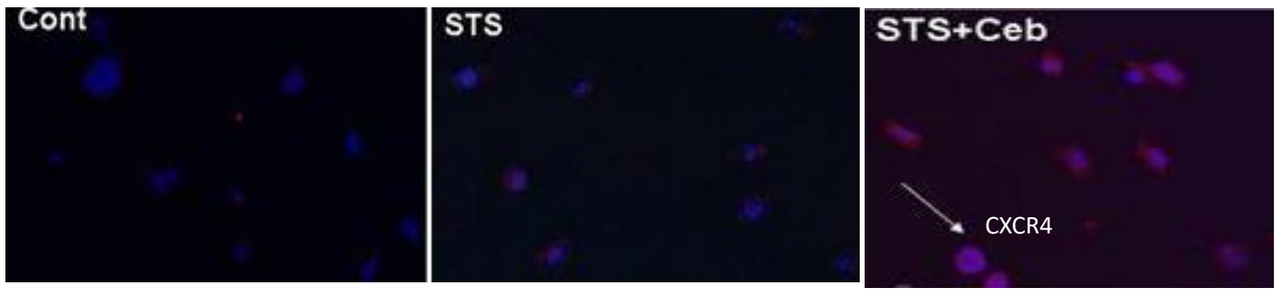
AIM

This work study whether Ceb may protect cortical neurons at 7 DIV against staurosporine-induced cell death or LPS-induced inflammation in cortical neurons at 7 DIV and N2a cell line.
For this purpose, extracts from cortical neurons or N2a cells were isolated and the expression o fseveral inflammatory mediators quantified by pCR (IL-1 beta and CXCR4/SDF1) axis

Cerebrolysin increases neurite length in cortical neurons at 7 DIV



Nuclear CXCR4 detection in staurosporine- N2a neuroblastome cell line under Staurosporine treatment



Cont: Neuroblastome N2a control cells (without treatments)

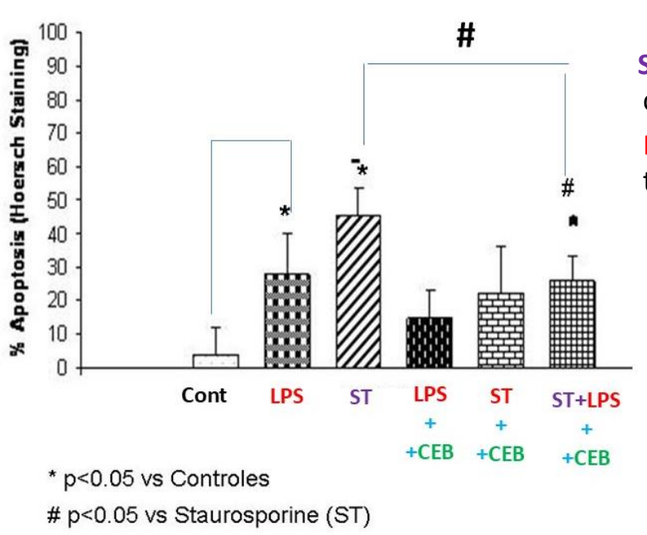
STS: Staurosporine N2a treated cells

ST: Staurosporine-treated N2a cell line

REFEREMCES

RESULTS

Antiapoptotic effects of cerebrolysin in staurosporine-treated cortical neurons at 7 DIV



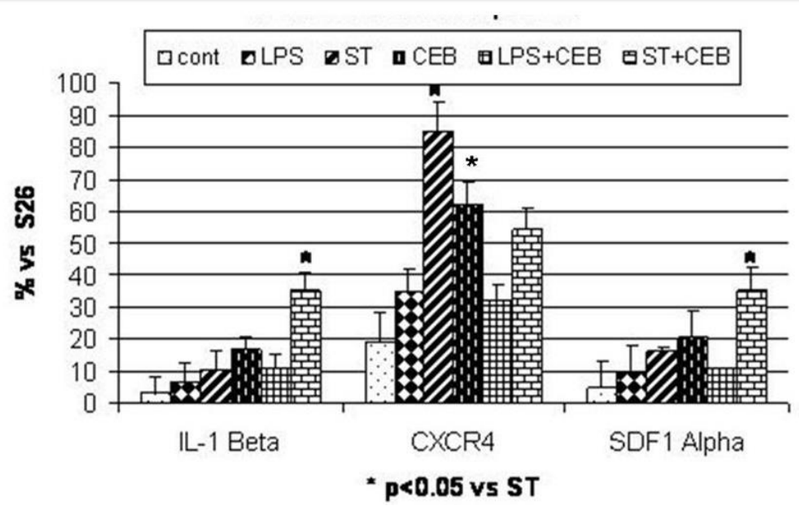
ST: Staurosporine treatment in cortical neurons (c.n) at 7 DIV.

LPS: Lipopolysacharide treatment in c.n at 7 DIV

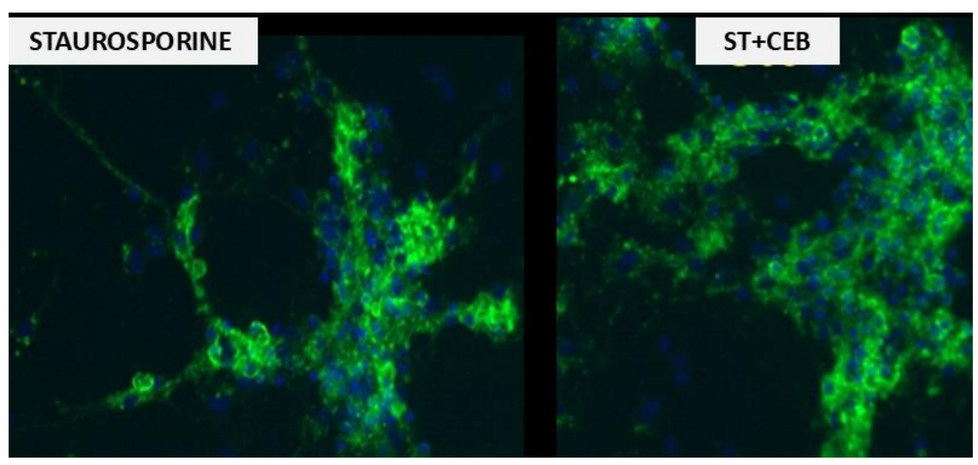
ST+Ceb: Staurosporine treatment in Ceb-treated cortical neurons at 7 DIV.

ST+**LPS**+**Ceb**: Staurosporine and Lipopolysacharide treatment in Ceb-treated c.n at 7 DIV.

Ceb meediated antiaoapoptotic effeccts by CXCR4 in cortical neurons under inflammation or apoptosis



Cerebrolysin increases PSA-NCAM levels in staurosporine-treated cortical neurons (7 DIV)



ST (Staurosporine): staurosporine (ST) treatment In cortical neurons at 7 DIV

ST+Ceb: Cerebrolysin-treated cortical neurons with Staurosporine (ST)

CONCLUSION

CEREBRROLYSIN INDUCES NEURAL PLASTICITY BY INCREASING PSA-NCAM PROTEIN LEVELS

CEREBRROLYSIN PREVENTS APOPTOSIS BY INCREASING CXCR4 IN –STAUROSPORINE-TREATED NEURONS AS WELL AS IN N2A TREATED CELLS

Schauer E, et al. Neuroprotection of cerebrolysin in tissue culture models of brain ischemia: p ost lesion application indicates a wide therapeutic window. J Neural Transm (Vienna). 2006 Jul;113(7):855-68.