

INTRODUCTION

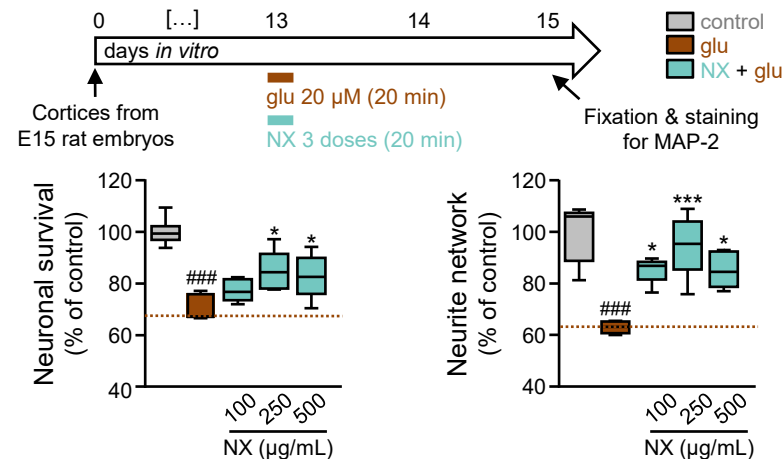
The subcommissural organ (SCO)-spondin is a brain-specific glycoprotein produced during embryogenesis, that strongly contributes to neuronal development. This organ becomes atrophic in adults, thereby losing protective functions of damaged nervous cells. Excitotoxicity is a common feature of CNS disorders/injuries, caused by an excessive stimulation of glutamate receptors leading to Ca²⁺ overload and neuronal death. Using rat and human neuron cultures, we evaluated the protective effect of NX peptide (Axoltis Pharma – France), an innovative drug candidate derived from the SCO-spondin, against glutamate neurotoxicity.

METHODS

Primary neurons were exposed to glutamate (glu) and treated with NX peptide. Two days later, rat neurons were immunostained with MAP-2 for assessment of neuronal survival and neurite network. One day later, human neurons were subjected to lactate dehydrogenase assay or to staining with TuJ1 or active caspases 3/7. The mechanism of action was investigated by exposing rat cortical neurons to β₁-integrin antibody and inhibitors targeting receptors and intracellular mediators that trigger apoptosis, neuronal survival, or neurite growth.

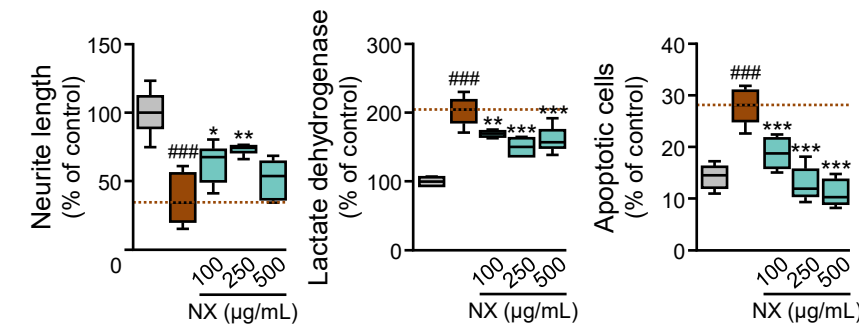
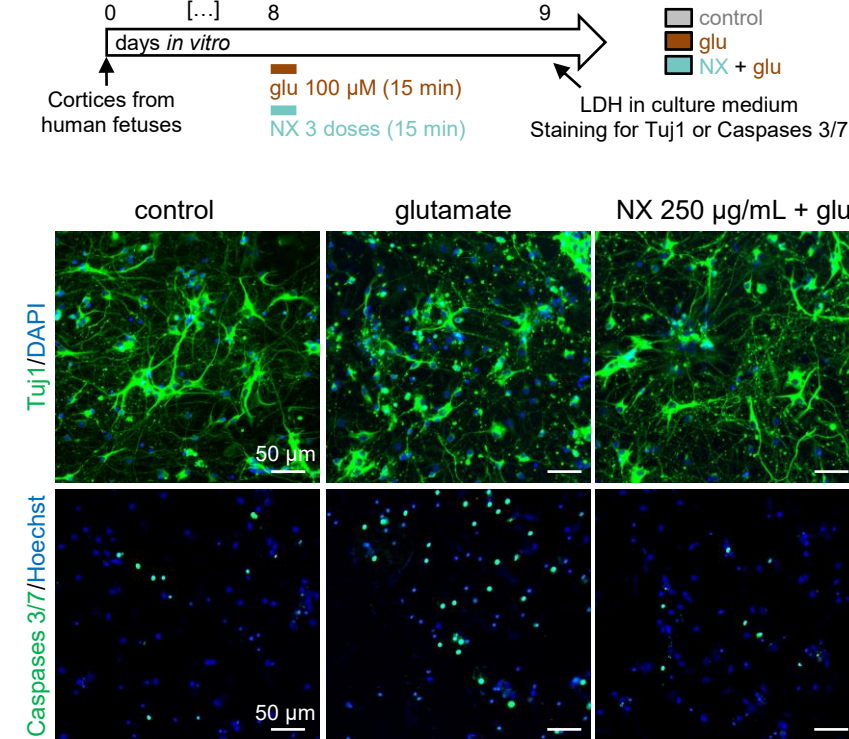
RESULTS

NX peptide protects rat cortical neurons from excitotoxicity



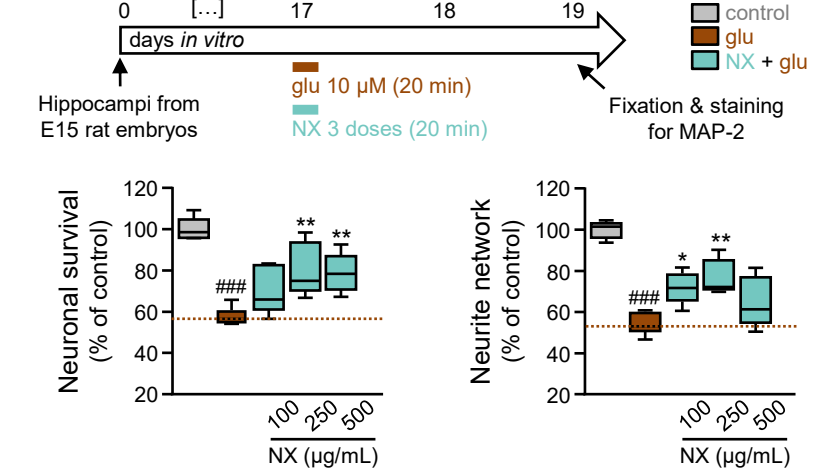
One way-ANOVA followed by Tukey's multiple comparisons test: ###p<0.001 control vs glu; **p<0.01, *p<0.05 glu vs NX/glu, n=5-6.

NX peptide protects human cortical neurons from excitotoxicity



One way-ANOVA followed by Tukey's multiple comparisons test: ###p<0.001 control vs glu; ***p<0.001, **p<0.01, *p<0.05 glu vs NX/glu; n=6.

NX peptide protects rat hippocampal neurons from excitotoxicity

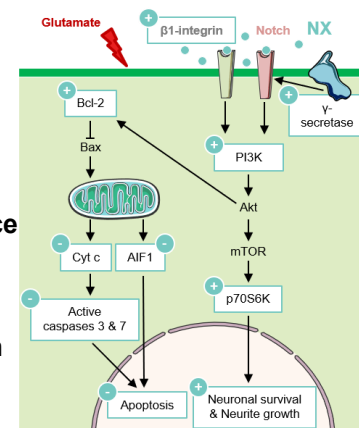


Kruskal-Wallis followed by Dunn's test: ###p<0.001 control vs glu; ***p<0.001, *p<0.05 glu vs NX/glu, n=5-6.

CONCLUSION

NX peptide is a promising drug candidate that significantly reduces glutamate-induced neurotoxicity (Delétage, Le Douce et al., Neuroscience, 2021).

Please check out our *in vivo* demonstration of NX efficacy in AD (P193) and ALS (P594)!



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