# A SUBCOMMISSURAL ORGAN-SPONDIN-DERIVED PEPTIDE (NX210c) IMPROVES RECOVERY OF SYNAPTIC TRANSMISSION AFTER ISCHEMIA *IN VITRO*

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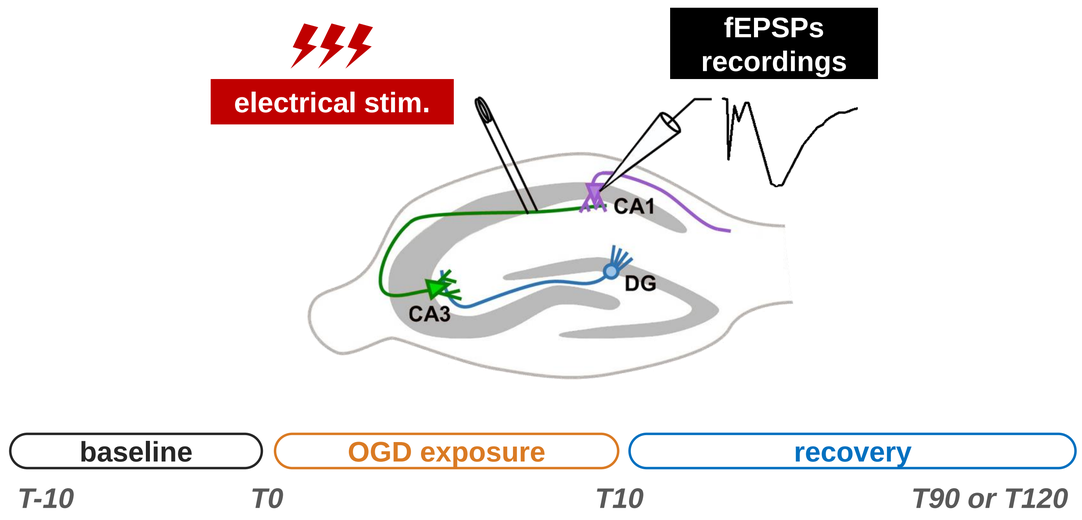
## INTRODUCTION

Although NMDA receptor is known to be involved in ischemic neuronal damage, its different subunits might activate opposite pathways. Indeed, GluN2B would more often promote excitotoxic cell death while GluN2A would rather activate neuroprotective signaling pathways.

Previously we showed that the subcommissural organ-spondin-derived peptide NX210c had neuroprotective effects *in vitro* and might act through GluN2A subunits. The aim of this study was thus to determine if NX210c could improve functional recovery after an acute ischemia *in vitro*.

## METHODS

Acute hippocampal slices from adult mouse were first superfused with artificial cerebrospinal fluid (aCSF) gassed with carbogen to reflect normoxia. After a 10 minutes baseline, slices were exposed to an episode of oxygen-glucose deprivation (OGD) followed by reoxygenation. NX210c (250 µg/mL) or vehicle was bath-applied either from the beginning or the end of OGD exposure. Functional recovery was assessed by recording field excitatory postsynaptic potentials (fEPSPs) evoked in CA1 by Schaffer collateral stimulation.

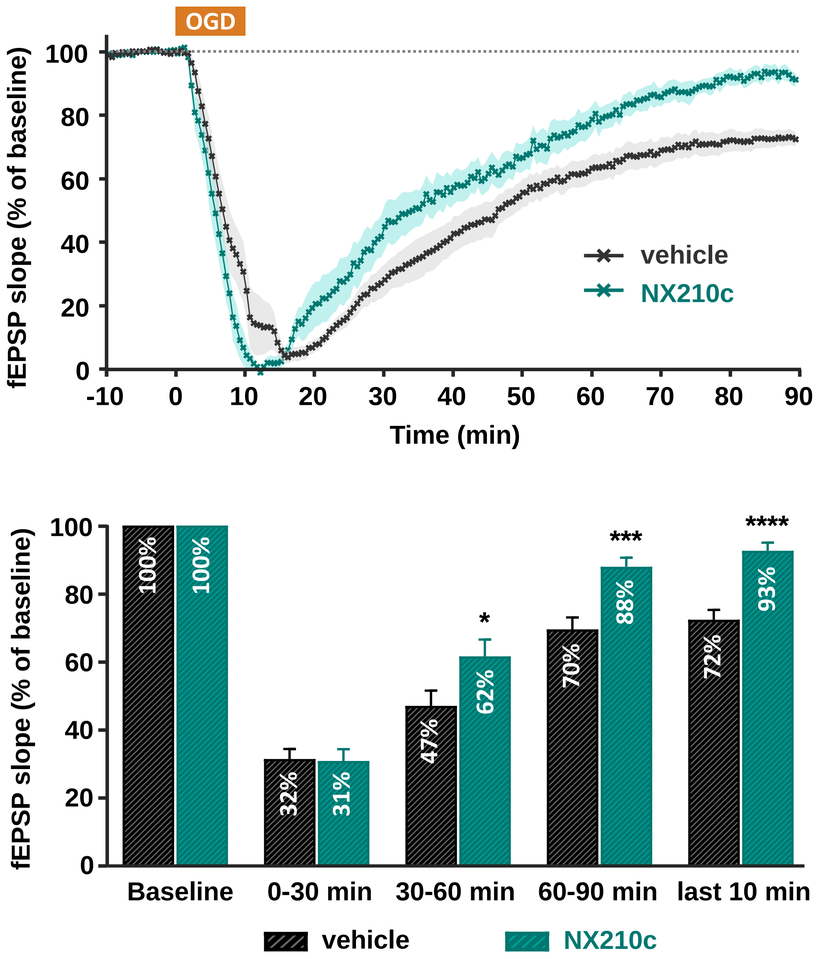



## RESULTS

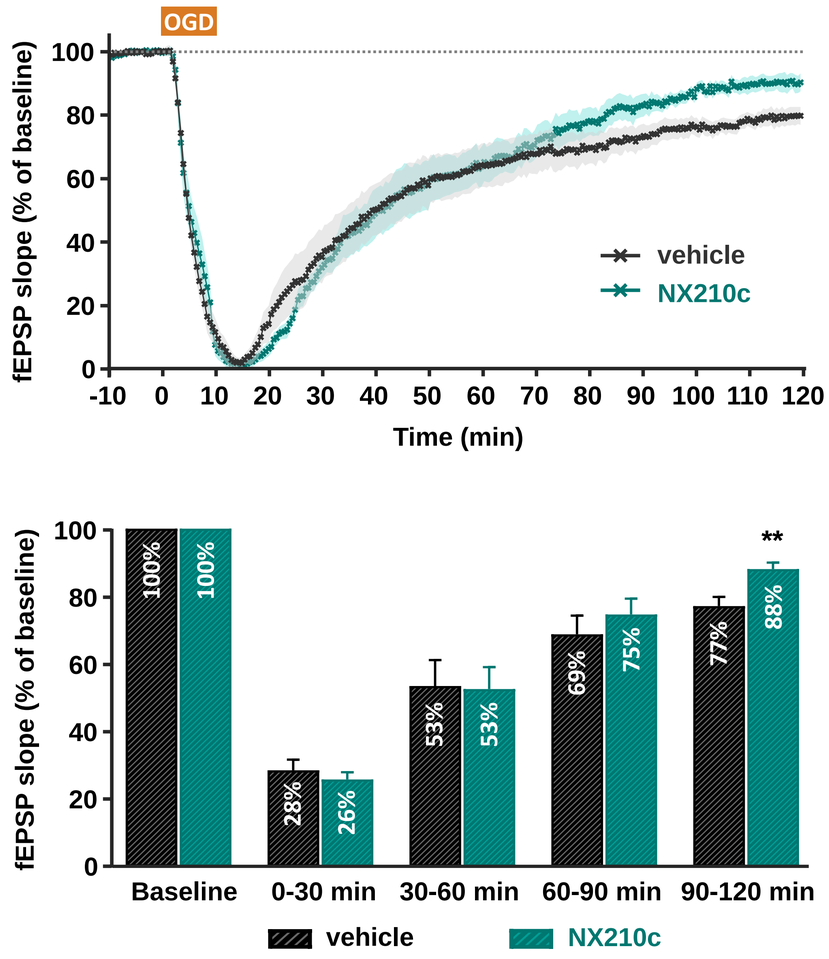
As expected, a substantial depression of synaptic transmission was observed in slices subjected to OGD. Concurrent administration of NX210c improved synaptic recovery, as shown by higher fEPSP slopes in NX210c- than in vehicle-treated slices within 30-60 minutes from OGD induction (fEPSP slopes as % change from baseline: 61.7±5.0 for NX210c *vs* 47.2±4.5 for vehicle, p<0.05, ❶).

This effect persisted until 60-90 minutes (88.0±2.6 for NX210c *vs* 69.6±3.5 for vehicle, p< 0.0001, ❶) and was even more striking during the last 10 minutes following OGD induction (92.6±2.4 for NX210c *vs* 72.4±2.9 for vehicle, p< 0.0001, ❶). NX210c was efficient even if added after OGD exposure (88.0±1.9 for NX210c *vs* 77.1±2.7 for vehicle at 90-120 minutes post-OGD, p<0.01, ❷).

### ❶ Early administration of NX210c




### ❷ Later administration of NX210c




## CONCLUSION

- NX210c allows a better synaptic recovery in an *in vitro* model of cerebral ischemia, regardless of when it is administered.
- NX210c is a promising drug candidate to alleviate the neurological sequelae of any condition that may result in brain ischemia, such as stroke, cardiorespiratory failure or low oxygen saturation level (notably observed in COVID-19 patients).

*Disclosures ►► MS, SL and JLD are employed by Axoltis, YG is the CEO, and a shareholder of Axoltis.*