Spinal cord blood flow elevation with systemic vasopressor noradrenaline is partly mediated by vasodilation of spinal arteries due to reduced expression of alpha adrenoreceptors

Seyar Entezari1,2, Mathias Møller Thygesen1,2, Christian Staehr3, Elizaveta Melnikova3, Mathias Skov1, Rajkumar Rajanathan3, Mads Rasmussen1,4, Mikkel Mylius Rasmussen1,2, Vladimir V. Matchkov3

1 1 Department of Clinical Medicine, Aarhus University, Aarhus, Denmark, 2 2 Department of Neurosurgery, CENSE SPINE, Aarhus University Hospital, Aarhus, Denmark, 3 3 Department of Biomedicine, Aarhus University, Aarhus, Denmark, 4 4 Department of Neurosurgery -Anesthesiology, Aarhus University Hospital, Aarhus, Denmark

## **Background:**

Following traumatic spinal cord injury (TSCI), guidelines recommend maintaining mean arterial pressure (MAP) at 85–90 mmHg using vasopressors such as noradrenaline (NA). Whether this improves spinal cord blood flow (SCBF), and how NA acts on spinal arteries, remains unknown.

## **Methods:**

The study included nine 38-42 kg landrace pigs. In six, MAP was gradually elevated with NA while SCBF was recorded by laser Doppler flowmetry. Spinal cord samples were excised for isolation of spinal cord arteries that were used for ex-vivo functional assessment in isometric myograph. Mesenteric arteries from three additional pigs were used as peripheral controls. Other spinal cord and mesenteric arterial segments from the same biopsies were snap-frozen for adrenoceptor's expression analysis with quantitative PCR.

## **Results:**

SCBF was significantly reduced at MAP <50 mmHg and increased within the MAP range of 50-100 mmHg (p=.02). No additional increases were observed at 100-150 mmHg (p=.15) or 150-200 mmHg (p=.51). However, SCBF significantly increased over the study time-course (at 80 min, p=.002; at 100 min, p<.001), consistent with cumulative NA exposure. Ex-vivo, isolated spinal arteries showed a tendency for vasorelaxation, abolished by  $\beta$ -adrenoceptor inhibitor, propranolol. In contrast, mesenteric arteries demonstrated  $\alpha$ -adrenoceptor-mediated contraction, which was potentiated by propranolol. Mesenteric arteries showed a higher

expression of  $\alpha 1A$  adrenoceptors than spinal arteries, while no significant difference was found in other adrenoceptor isoforms.

## **Conclusions:**

We showed that SCBF increases at MAP 50–100 mmHg but not beyond. We also showed that NA increases SCBF in-vivo and relaxes spinal arteries ex-vivo. This effect was associated with a low arterial expression of  $\alpha$  adrenoceptors over  $\beta$  adrenoceptors in the spinal cord.