Adropin as a novel protective factor after subarachnoid hemorrhage

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Introduction

- Hemorrhagic stroke is a devastating disease with a multifaceted pathology[1].
- Cerebral edema, blood-brain barrier disruption, and cerebral vasospasm are hallmark features of subarachnoid hemorrhage (SAH)[1].
- Adropin is a novel peptide that is highly expressed in brain tissue and is known to regulate endothelial cell function[2,3].

Objectives

- We tested the hypothesis that adropin treatment would protect against acute brain injury and delayed cerebral vasospasm following subarachnoid hemorrhage.
- Cerebral edema, blood-brain barrier permeability,, microthrombi formation, and microglial activation were evaluated at 24 hours post-SAH.
- Middle and anterior cerebral arteries were measured at 7 days post-SAH.

Results

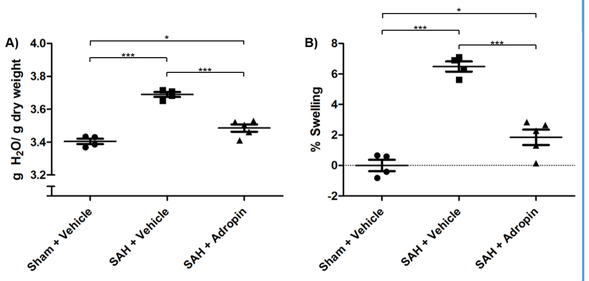

Figure 1. Adropin protects against cerebral edema following SAH. SAH + vehicle induced 6.49% cerebral swelling compared to sham surgery (p<0.001). Adropin-treated mice had significantly lower swelling than the vehicle group but remained higher than control (1.84% swelling, p<0.001 vs SAH + vehicle, p<0.05 vs sham surgery).

Results

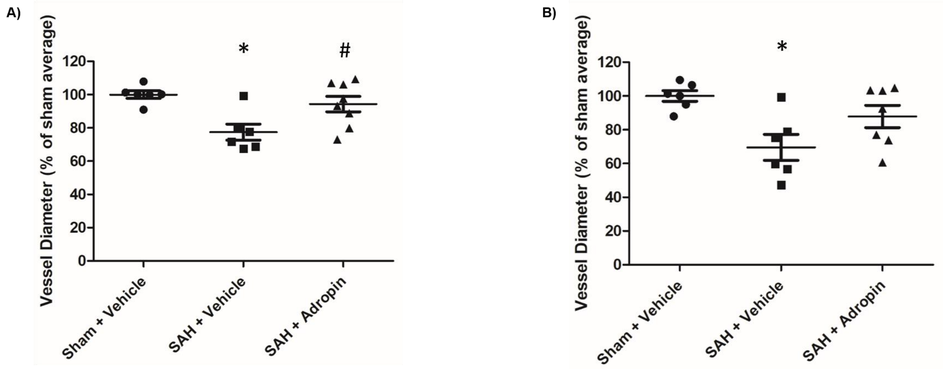

Figure 2. Cerebral artery diameter 7 days post-SAH. A) Middle cerebral artery measurements, SAH + vehicle: 77.4% of sham average, SAH + adropin: 94.32% of sham average. **B)** Anterior cerebral artery measurements, SAH + vehicle: 69.53% of sham average, SAH + adropin: 87.89% of sham average. * p<0.05 compared to sham, # p<0.05 compared to SAH + vehicle.

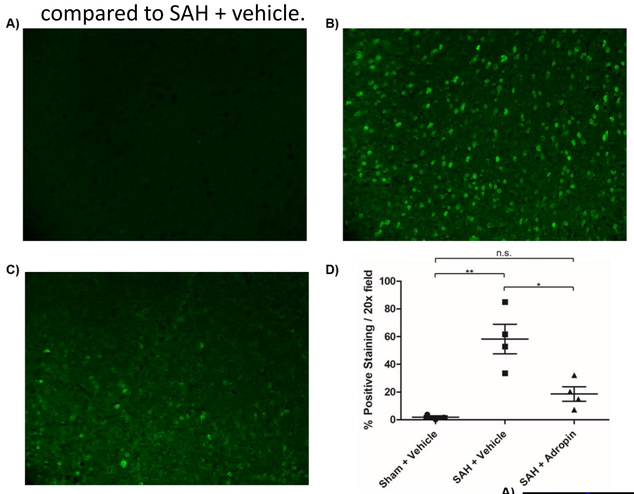

Figure 3. Adropin reduces fluorescein extravasation at 24 hours post-SAH. SAH (B) significantly increased the permeability of sodium fluorescein (58.32% positivity vs 1.84%, p<0.01). Adropin treatment (C) reduced this effect (18.2% positivity, p<0.05 compared to SAH + vehicle).

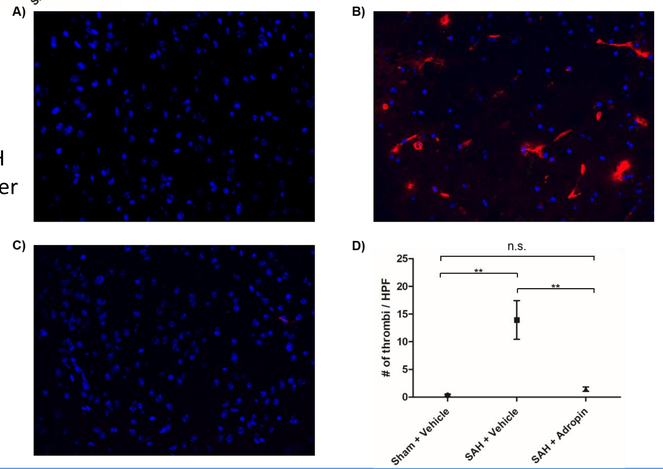

Figure 4. Adropin treatment inhibits microthrombi formation following SAH. SAH + vehicle mice (B) had 13.94 microthrombi per high-powered field compared to 0.31 in the sham surgery group (A), p<0.01. Adropin treatment (C) significantly reduced the number of microthrombi compared to vehicle-treatment (1.44 thrombi per HPF, p<0.01).

Results

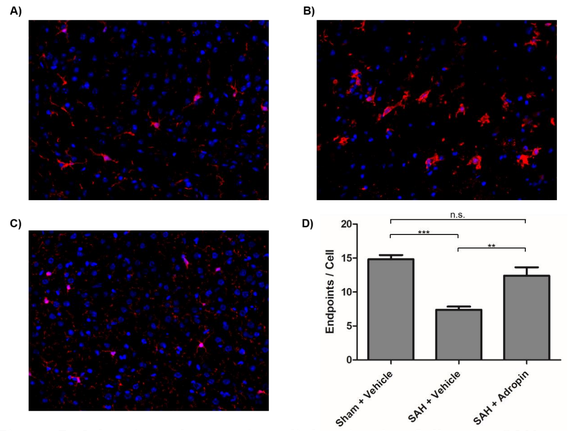

Figure 5. Adropin reduces microglial activation following SAH. SAH + vehicle treatment caused significant reduction in endpoints/cell of microglia (7.38 vs 14.82 endpoint/cell, p<0.001). Adropin treatment reversed this effect (12.41 endpoints/cell, p<0.01 compared to vehicle).

Conclusions and Future Directions

- Our preliminary data are consistent with the hypothesis that adropin protects against both early brain injury and delayed cerebral vasospasm.
- We have demonstrated that adropin is beneficial in both the acute and delayed timeframes following SAH
- Future work will investigate the mechanisms by which adropin exerts its protective effects.

References

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Acknowledgements

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