THE RENIN-ANGIOTENSIN SYSTEM AND VOLUME REGULATION IN LAMPREYS

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EXTENDED ABSTRACT ONLY- DO NOT CITE

Some species of lampreys are anadromous migrants between (FW) and seawater (SW) and adjust ionic and osmoregulatory mechanisms in a similar way to teleost fish (Rankin, 1997). Hyper-osmoregulation in FW demands excretion of large volumes of urine, whilst hypo-osmotic regulation in SW depends on increasing drinking and drastically reducing urine output. Endocrine control of body fluid volume and composition in lampreys is poorly understood and existence of a lamprey renin-angiotensin system (RAS) has until recently been in doubt (Henderson *et al.*, 1993). This endocrine system plays a key role in regulation of cardiovascular function and blood volume homeostasis in many vertebrates and is involved in survival of teleost fish in high external salinities.

Recent isolation and sequencing of endogenous angiotensin I (Ang I) in *Lampetra fluviatilis* and *Petromyzon marinus* (Rankin, Watanabe, Nakajima and Takei, unpublished) led to our measurement of the physiologically active angiotensins (angiotensin II and III: Ang II & III) (Rankin *et al* 2001). In these studies, *Lampetra fluviatilis* showed higher levels angiotensins in SW than in FW. Our more recent studies have aimed to investigate the activation of the RAS and its possible role in regulation of renal function.

Adult lampreys (*Lampetra fluviatilis* L.) were caught in Ringkøbing Fjord, Denmark at the start of their migration into FW and held either in FW or

gradually-acclimated to hyperosmotic environments (Brown and Rankin, 1999) where they were held for ~ 3-5 weeks.

Investigation of the activation of the renin-angiotensin system

A range of approaches were employed including blood volume depletion of lampreys acclimated to 21ppt (~40% blood volume removal), isotonic volume loading of FW-acclimated lampreys (1% body weight ip), salt loading of FW-acclimated lampreys (4M NaCl, 1% body weight ip,) and rapid changes in environmental salinity (FW to 605 mOsm/kg; 758 mOsm/kg to FW). Circulating angiotensins were determined by radioimmunoassay after collection of blood samples from the caudal vasculature of MS222-anaesthetised fish.

Measurement of circulating angiotensins showed a rapid activation of the RAS after volume depletion (Fig 1). In agreement with the activation of the RAS by hypovolaemia (or the resultant hypotension), ip injection of isotonic saline (1% body wt) resulted in rapid decline of plasma angiotensins (within 15 min post-injection, $P<0.01$) followed by restoration to control levels 30 and 60 min post-injection. However, regulation of the RAS appears to involve interaction of volume receptors and osmoreceptors since injection of hypertonic saline, (again at 1% body wt) which raised plasma osmolality compared to injection of isotonic saline within 15 min ($P<0.01$), did not affect plasma angiotensins.

Transfer of lampreys from 70% SW to FW which significantly lowered plasma osmolality and might be predicted to cause acute volume expansion was associated with a significant decline in plasma angiotensins ($P<0.05$) after 24h, although plasma angiotensins returned to a concentration not dissimilar from those in 70% SW after 7 days. After acute transfer from FW to 60% SW, the significant rise in plasma osmolality and predicted volume depletion was associated with rising plasma angiotensins. These results imply that volume receptors exert dominant control of the RAS

Renal Effects of Angiotensin II infusion

The renal effects of [Asp^1 Val^5]Ang II were determined by intravenous infusion of anaesthetised *Lampetra fluviatilis* with 10^{-10} or 10^{-9} moles min^{-1} kg body wt^{-1} (n=4 and 5 respectively) and serial collection of urine samples

(as described by Brown & Rankin, 1999). Both doses of Ang II led to a decline in urine flow rate with a significant decline in urine output after 40 min of 10^{-9} moles min^{-1} kg $body^{-1}$ (Fig 2). Preliminary studies also indicated that Asn^1-Val^5-Ang II at 1 to 1.6 x 10^{-9} moles min^{-1} kg body wt^{-1} exerts an antidiuretic action in the sea lamprey, *Petromyzon marinus*.

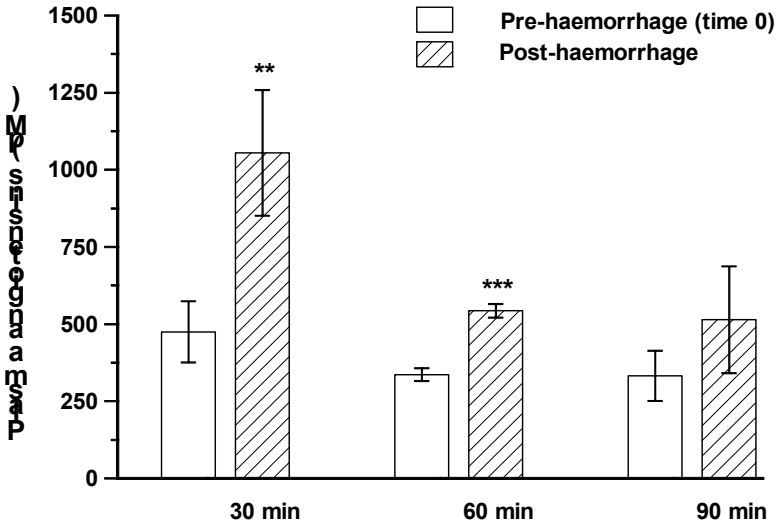

Fig 1. Plasma angiotensins (pM) in lampreys acclimated to 21ppt, 576 mOsm kg^{-1} prior to a haemorrhage and 30min (n=10), 60min (n=11) or 90 min (n=7) after removal of 40% blood volume. Data are means $\pm$ SE; ** P< 0.01, *** P<0.001, paired t tests.

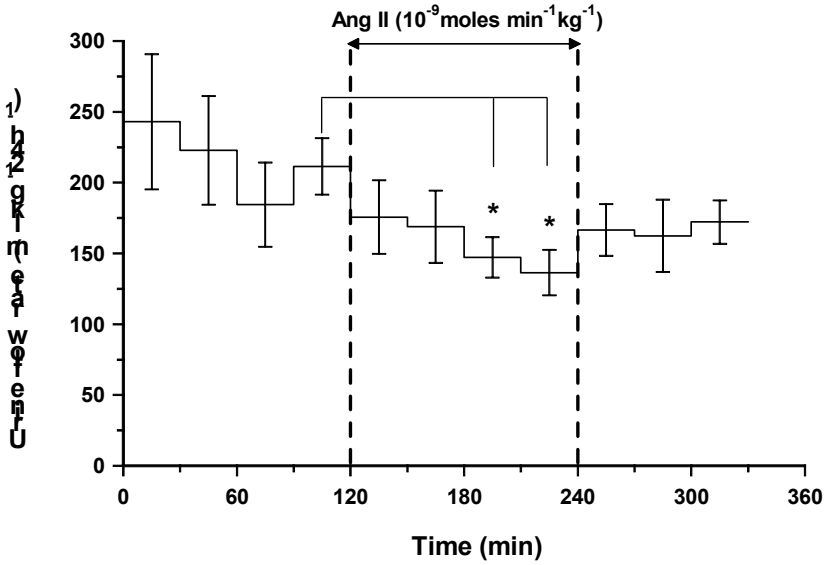

Figure 2. Effect of Ang II on urine flow rate of the river lamprey, *Lampetra fluviatilis*, (n=5) infused with saline via the posterior cardinal vein (2µl min^{-1} kg body wt^{-1}) for 2h control period, saline containing Ang II at 10^{-9} moles min^{-1} kg body wt^{-1} for 2h and then returned to a saline infusion.

In summary, the newly-discovered renin-angiotensin system of the river lamprey appears to be activated by volume receptors. This is in keeping with the vasoconstrictor action and antidiuretic actions of Ang II.

References

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Acknowledgments

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