# A COMPARISON OF THE HYPOTENSIVE EFFECTS OF CGRP AND ADRENOMEDULLIN IN ANAESTHETISED MICE

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CGRP and the structurally related peptide adrenomedullin (AM) have profound depressor effects on blood pressure, which are thought to be mediated through receptors composed of G-protein-linked calcitonin receptor-like receptors (CL) with receptor activity-modifying proteins (RAMP; McLatchie et al. 1998). Although the hypotensive effects of exogenous CGRP and AM have been well characterised in many species, to date there have been no such studies reported in the mouse. In the present study, the hypotensive effects of exogenous CGRP and AM were assessed and compared side-by-side in naturally ventilated CD1 mice, anaesthetised with urethane (2.5mg/g, i.p.). Drugs were administered as a bolus injection (100µl) into the jugular vein and consequent effects on blood pressure were monitored via a cannula (OD<0.7mm) that was inserted into the carotid artery and connected to a blood pressure transducer and PowerLab data acquisition system.

Baseline mean arterial pressure was 53 $\pm$ 5mmHg (n=7). Both CGRP and AM produced dose-dependent decreases in blood pressure (Figure 1) with similar latencies for maximal effect (~2min) and duration of action (~10min). Although CGRP proved to be approximately 100 fold more potent than AM ($ED_{50}$=3.2pmol for CGRP compared with 345pmol for AM), the maximal depressor effect for CGRP was lower than that for AM (% hypotension from baseline, 19.1 ± 2.9 for CGRP compared with 27.7 ± 1.6 for AM). When 2 repeated injections of a single dose of either CGRP (10pmol) or AM (1000pmol) were administered, the second response to CGRP was identical to the first, even when the injection interval was as small as 15 min. In contrast, the second response to adrenomedullin was attenuated compared with the first response for at least a 3 h.

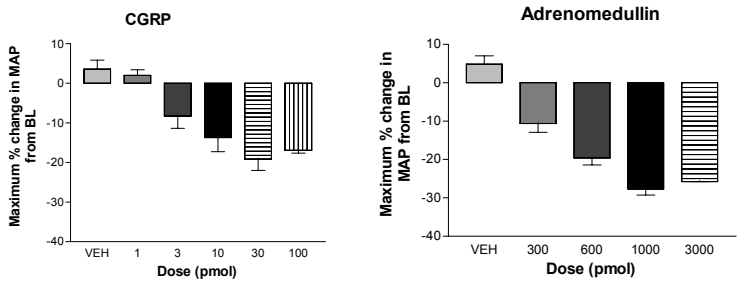


*Figure 1: Effect of CGRP (left) and adrenomedullin (right) on mean arterial pressure in CD1 mice. Data shown as mean $\pm$ s.e.m., n=4/group.*

These data demonstrate the dose-related ability of exogenous CGRP and AM to act as hypotensive agents in the mouse. In addition these data further highlight differences in the nature of the hypotension evoked by CGRP compared with AM. Future studies will focus on characterising the receptors that mediate these responses through use of available antagonists for CGRP (CL/RAMP1) and $AM_1$ (CL/RAMP2) receptors as well as genetically modified mice.

McLatchie et al., (1998). Nature, 393, 333-339.