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IMPAIRED VASCULAR RESPONSES TO CALCITONIN GENE-RELATED PEPTIDE IN THE AGEING α-CGRP KNOCKOUT MOUSE

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Calcitonin gene-related peptide (CGRP) is a potent microvascular vasodilator derived predominantly from perivascular sensory neurones. It has been suggested that vascular reactivity to CGRP is diminished with increasing age whilst levels of CGRP are also thought to decline. Our aim was to investigate how vascular responses to CGRP changed with age in α-CGRP wild type (WT) and knockout (KO) mice. Male and female α-CGRP WT and KO mice were aged to 15 months at which point mice were killed and second order mesenteric arteries were mounted in a wire myograph. Aortic tissue was collected and mRNA expression of CGRP receptor subunits was evaluated by RTqPCR. Data were analysed by ANOVA and Student's t test, where appropriate.

Maximal relaxation to CGRP (100 nM) in aged WT mice produced a 75.30±7.48% relaxation from initial tone induced by 10 nM U46619. Conversely, maximal relaxation to CGRP in aged KO vessels produced a 31.33±8.74% decline in tone, an effect found to be significantly different ($p<0.01$). Analysis of gene expression of CGRP receptor subunits (calcitonin receptor-like receptor, receptor activity modifying protein 1 and receptor component protein) found a general trend towards an increase in expression within the aortic wall. This study has shown that whilst vascular reactivity to CGRP is diminished with advancing age, it does not appear to be as a result of decreased receptor expression.

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