GENE EXPRESSION OF NERVE GROWTH FACTOR IN THE DEVELOPING SPONTANEOUSLY HYPERTENSIVE RAT

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by

Patrick Helmer James Falckh B.Sc.(Hons.)

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ABSTRACT

Hypernoradrenergic innervation of the vasculature is a recognised as a key characteristic in the spontaneously hypertensive rat (SHR), a genetic animal model of hypertension. Nerve growth factor (NGF), a protein essential for the development and maintenance of sympathetic innervation, has been shown to be elevated in the young SHR when compared to the normotensive control, the Wistar-Kyoto (WKY) rat. NGF concentrations have been shown to correlate with gene expression for the protein and with the degree of sympathetic innervation in many species. The NGFmRNA levels in cardiovascular tissue of neonatal, and developing, SHR and WKY rats were investigated to determine if there is a link between the gene expression of NGF and the pattern of abnormal sympathetic innervation in this model.

The reliability of the cDNA probe used for the determination of NGFmRNA concentrations was initially verified by investigating NGFmRNA concentrations in the submaxillary salivary gland of the mouse after pharmacological manipulation.

Mesenteric and caudal arteries of the SHR were found to contain significantly elevated levels of NGFmRNA (> 5 fold) consistent with the hypernoradrenergic state reported for these blood vessels. The kidney of the SHR also displayed an elevated NGFmRNA production, consistent with the elevated innervation reported for this tissue. Cardiac and aortic tissues, which do not exhibit hypernoradrenergic innervation in the SHR, displayed low levels of NGFmRNA which were generally similar to levels seen in cardiac and aortic tissues from WKY rats. In the hypernoradrenergically

innervated tissues the NGFmRNA levels were elevated as early as 2 days of age and the elevated level sustained for 6 weeks. The latter period corresponds to the normal time course for sympathetic innervation of the vasculature.

It is proposed that the elevated degree of innervation seen in resistance vessels and organs (for example in the kidney) is due, in part, to a sustained elevation of NGFmRNA and that the elevated NGFmRNA is present at birth. The findings also provide a rational basis for the elevated noradrenaline (NA) content of vessels in the SHR, the larger releasable pool of NA in the SHR and the elevated levels of NGF peptide in vessels from the SHR. The results provide sufficient stimulus for examination of a role of NGF in the initiation of hypertension in the SHR.

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