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Professorial Research Fellow in Physiology

Area of research

Mechanisms of neurogenic hypertension

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Summary

Paton's group seeks to understand what changes within the central nervous system during the aetiology of neurogenic hypertension. Sympathetic nerve activity destined for the heart and arterioles is elevated prior to the onset of hypertension, which is suggestive of a causative role. In hypertension, cerebral vascular resistance is elevated causing brain hypoperfusion - a well known stimulant of sympathetic activity and hypertension. The microvasculature of the brainstem is also inflamed.

The hypothesis of elevated brainstem vascular resistance and inflammation as causative to hypertension is being explored in animal models and human patients. Transcriptomic analysis of brainstem genes altered in hypertension has led to exciting novel targets that are being validated with virally mediated transgenesis, stem cell transplantation, optogenetics and radio-telemetry *in vivo*.

The group's interest in mechanisms of central respiratory pattern generation has led to the observation that its modulation of sympathetic outflow is enhanced in hypertension. Additionally, data has shed light on plausible reasons for respiratory arrhythmias such as: sudden infant death and Rett syndromes. Data are being used to make mathematical models to assist in the further understanding of brainstem function as well as contributing to the Human Physiome project. A number of clinical translational studies driven by hypotheses gleaned from basic animal research are now underway in hypertensive patients.

Activities / Findings

- 1995-1996: Invention of a "tour de force" integrative physiological *in situ* *working heart- brainstem preparation*. This allowed studies we could not have done previously.
- 1998-2002: In collaboration with Professor Sergey Kasparov, we revealed that brainstem actions of angiotensin II, a peptide associated with hypertension, were mediated by liberation of nitric oxide from the endothelium leading to a novel form of brain signalling: *vascular-neuronal signalling*.
- 2003: We provided unequivocal evidence that *vascular-neuronal signalling* in the brainstem contributed to high blood pressure levels in an animal model of hypertension.
- 2006-present: Discovery that brainstem pacemaker activity was essential for gasping. This and other work dives our mathematical modelling which contributes to the *Human Physiome Project*.
- 2007- present: In collaboration with Professor David Murphy, we identified unique genes within brain regions regulating arterial pressure thereby providing unique clues as to those that may generate neurogenic hypertension.
- 2007: We discovered that the brainstem vasculature was inflamed in the hypertensive brain.
- 2007: In collaboration with Professors Jeff Smith (NINDS, NIH) and Ilya Rybak (Drexel University), we revealed the precise compartments of the brainstem for generation of distinct respiratory patterns and the conditions and mechanisms for expression of these different rhythms.

2009: In collaboration with Dr Andrew Allen (Melbourne University) and Dr Anthony Pickering, we discovered that enhanced sympathetic activity precedes the onset of hypertension and is dependent on exacerbated modulation by the brainstem respiratory pattern generator.

Teaching

- Respiratory physiology to Veterinary, Medical and Science students.
- Respiratory practical classes.
- Third year honours element organiser on the Cardiovascular System in Health and Disease.
- Cardiovascular physiology to stage III honours physiology students
- Molecular Neuroscience course
- Lectures on cardiovascular physiology to students at the University of Oxford.

Keywords

- Brainstem
- autonomic nervous system
- sympathetic activity
- blood pressure
- breathing
- baroreceptor
- chemoreceptor
- reflexes
- bladder

Skills

- Hypertension
- neurovascular disease
- cerebral artery stenosis
- SIDS
- Rett syndrome
- heart failure

Processes and functions

- Autonomic nervous system function
- homeostatic reflexes

Methodologies

- Neurophysiology
- patch clamp
- imaging
- fMRI
- microneurography
- in vivo gene transfer
- lentivirus
- adenovirus
- stem cell

Memberships

Organisations

[School of Physiology, Pharmacology & Neuroscience](#)

Other sites

- [Bhi](#)
- [Neuroscience](#)

Research Areas

- [Neural control of cardiovascular & respiratory function](#)

Links

-  [home page](#)

Recent publications

- Oliver, EH, Pope, C, Clarke, E, Hewer, CL, Ogunniyi, AD, Paton, JC, Mitchell, T, Malley, R & Finn, A, 2019, [Th17 responses to pneumococcus in blood and adenoidal cells in children](#). *Clinical and Experimental Immunology*, vol 195., pp. 213-225
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- Roloff, Ev, Walas, D, Moraes, DJ, Kasparov, S & Paton, JF, 2018, [Differences in autonomic innervation to the vertebral arteries in spontaneously hypertensive and Wistar rats](#). *Journal of Physiology*, vol 596., pp. 3505-3529
- Rodrigues, JC, Erdei, T, Dastidar, AG, Szanthy, G, Burchell, AE, Ratcliffe, LE, Hart, EC, Nightingale, AK, Paton, JF, Manghat, NE & Hamilton, MC, 2018, [Left ventricular extracellular volume fraction and atrioventricular interaction in hypertension](#). *European Radiology*.
- Magalhaes, K, Spiller, P, Da Silva, MP, Kuntze, L, Paton, J, Machado, B & Moraes, DJ, 2018, [Locus Coeruleus as a vigilance centre for active inspiration and expiration in rats](#). *Scientific Reports*, vol 8.
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- Barnett, WH, Jenkin, SEM, Milsom, WK, Paton, J, Abdala, AP, Molkov, YI & Zoccal, D, 2018, [The Kölliker-Fuse orchestrates the timing of expiratory abdominal nerve bursting](#). *Journal of Neurophysiology*, vol 119., pp. 401-412
- McBryde, F, Liu, B, Roloff, E, Kasparov, S & Paton, J, 2018, [Hypothalamic paraventricular nucleus neuronal nitric oxide synthase activity is a major determinant of renal sympathetic discharge in conscious Wistar rats](#). *Experimental Physiology*.

[View complete publications list](#) in the University of Bristol publications system

Networks & contacts

Bristol:

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 Dr Andreas Baumbach (Bristol Heart Institute)
 Prof Alan Champneys (Mathematical Engineering)
 Dr Kimberly Connor (Physiology & Pharmacology)
 Dr David Cussans (Physics)
 Prof S Kasparov (Physiology & Pharmacology)
 Dr Patrick Kehoe (Frenchay - Bristol)
 Dr Philip Langton (Physiology & Pharmacology)
 Professor Seth Love (Frenchay Hospital - Bristol)
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 Prof. D. Murphy (LINE - Bristol)
 Prof David Newbold (Physics - Bristol)
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