HUMAN NEUROTRANSMITTERS

The sympathetic nervous system has moved towards centre stage in cardiovascular and cardiometabolic disease. Using biochemical and nerve recording techniques our clinical investigations focus on the role played by the sympathetic nervous system in disease development and progression.

Research Brief
Cardiovascular neuroscience in several guises remains the focus of our group. Our projects are associated with four research themes: psychological stress, obesity, hypertension, and orthostatic intolerance. While these projects may appear disparate they are fundamentally linked, both in terms of the significant comorbidity that they share and that the underlying pathologies are initiated and sustained by disturbances in sympathetic regulation. Studies in depression aim to identify the consequences of sympathoexcitation and to develop novel cardioprotective strategies in this high risk patient group. In obesity and the metabolic syndrome we are investigating sympathetic dysfunction along the diabetic continuum and are examining the benefits of weight loss within different strata of metabolic risk. Our program in obesity also includes studies in young obese subjects, in those undergoing bariatric surgery, and we are initiating clinical trials with central sympathetic suppression in patients with polycystic ovary disease and in patients medicated with antipsychotic drugs who are subject to weight gain. In orthostatic intolerance we are extensively examining the sympathetic nerve biology in the two clinical variants of vasovagal syncope, those with very low or those with normal supine blood pressure.

Methodologies
- Assessment of sympathetic activity (noradrenaline spillover, microneurography, vein biopsies)
- Biochemical techniques - HPLC, ELISA, RIA, Western’s, SNP analysis
- Measures of insulin sensitivity (euglycaemic-hyperinsulinaemic clamp, OGTT)
- Human physiology (BP, HR, HRV, baroreflex, endothelial function, DEXA)
- Psychometric evaluation (patient interviews for depression, anxiety etc)

Selected Publications
**Diagnostic Profiles in Postural Syncope during Head Up Tilt Testing**

Heart rate, blood pressure and muscle sympathetic nerve activity in response to head up tilt in: (A) healthy subject, and patients with (B) the postural orthostatic tachycardia syndrome (POTS), (C) vasovagal syncope and (D) pure autonomic failure. By combining physiological measures the differing aetiology of forms of fainting can be clearly demonstrated.

**Sympathetic Nervous Activation in Obesity & Hypertension**

DEXA scan demonstrating increased abdominal obesity (left) and the association between increased BMI and muscle sympathetic nerve activity and blood pressure (right). Abdominal fat mass is a major driver of sympathetic activation.

**The Link between Brain Serotonin, Serotonin Transporter Genotype & Sympathetic Activity in Patients with Depression**

A marked sympathetic nervous activation is present in around 30% of patients with major depressive disorder (right). Using high internal jugular venous blood sampling we were able to quantify brain serotonin turnover (left) and demonstrate an association between serotonin transporter genotype, serotonin turnover (centre) and the degree of sympathetic activation.