Autonomic function in normal pregnancy: the role of studying heart rate variability

A well controlled interaction between the sympathetic and the parasympathetic system is necessary for adapting the cardiovascular system to various haemodynamic needs not only under pathophysiological circumstances, such as haemorrhage and shock, but also in physiological states such as pregnancy. Accordingly, alterations in autonomic cardiovascular control have been implicated to play an important aetiological role in certain diseases. Thus, as early as almost three decades ago, the development of hypertension in pregnancy has been associated with a loss of autonomic baroreflex control [1]. Methods for the clinical assessment of autonomic circulatory control in humans have therefore been of great interest for researchers involved in the field of cardiovascular physiology in pregnancy. For example, sympathoadrenergic activity was formerly evaluated mainly by means of venous, urinary or arterial catecholamine measurements. Providing inconsistent results, however, catecholamine concentrations cannot be taken any longer as reliable markers of sympathetic system activity in pregnancy. The reason for that is the fact that the rate of noradrenaline overflow to plasma is determined not only by the rate of noradrenaline release (and hence sympathetic nerve firing rate and nerve density), but also by the activity of the competing disposition mechanisms of uptake, metabolism, and diffusional flow to circulation. The latter is influenced by factors such as regional blood flow and the exchange conductivity of the capillary and post-capillary venular bed. In contrast, direct recordings of efferent post-ganglionic sympathetic activity to skeletal muscle by microneurography allow a precise, quantitative, and reproducible assessment of sympathetic neural vasoconstrictor activity [2].

A limitation of the microneurographical technique, however, is the fact that sympathetic outflow to skeletal muscle may not reflect sympathetic activity in other organs such as the heart and kidneys, which are equally important for autonomic circulatory control. Another recent technical advance for evaluating cardiovascular autonomic control in humans has been the introduction of power spectral analysis of heart rate variability, a marker of cardiac sympathetic activity [3]. Determination of the cyclical changes of heart rate over time does not only allow an assessment of sympathovagal control of the sinuatrial node under resting conditions but also enables researchers to non-invasively explore baroreflex mechanisms especially when spectral analysis of blood pressure variability is obtained simultaneously. Compared with the classical pharmacological method of arterial baroreflex testing, this newer technique, due to its non-invasive nature, represents a real advantage for studying pregnant women as it is safe and can be performed easily and repeatedly.

In this issue of Clinical Science, Blake et al. [4] demonstrate their results of longitudinal measurements of pulse interval and blood pressure variability obtained by spectral analysis during normal pregnancy at rest and in response to orthostatic stress. Their major new finding is that under supine conditions advancing gestation leads to a decrease in baroreceptor sensitivity for heart rate, most likely due to a decrease in vagal, rather than to an increase in sympathetic, tone. The reason for the observed decrease in high-frequency pulse interval variability, however, remains unclear from these studies. While mechano-electrical feedback due to volume related stretch of the sino-atrial node could potentially account for these changes, alterations in autonomic nervous system function may be possible as well. In support of the former hypothesis, reliable measures of plasma volume that can be performed safely and repeatedly over time in pregnant women would be needed; certainly not an easy task in this particular group of subjects. The latter hypothesis, which proposes an alteration of autonomic baroreflex control, could be investigated in more detail if one applied other existing techniques that incorporate different aspects of the neuroeffector mechanism such as microneurography. A single isolated aspect of autonomic function may misrepresent the true relationship between sympathetic nerve firing, sympathovagal balance and functional response.

As baroreceptor sensitivity for heart rate did not change significantly during standing but only in the supine position, this finding by Blake and colleagues may be interpreted in the sense that cardiac, but not arterial, baroreflex mechanisms may be perturbed with advancing gestation. To examine more clearly the impact of cardiac versus arterial baroreflex mechanisms, studies applying lower body negative pressure (LBNP) may be helpful. The LBNP method is a non-invasive method that, if low levels are applied, allows selective perturbation of the cardiac baroreceptors without affecting arterial baroreceptors and can be performed safely in pregnant women. Furthermore, as altered responses in individual cardiovascular reflex tests do not allow the exact location of the site of change (afferent, central or efferent), a number of different tests should be performed in order to obtain more precise information on the role of the
different limbs of the reflex arc. Thus, other commonly used standardized and validated non-invasive methods to study autonomic function in human pregnancy are the Valsalva manoeuvre, the isometric handgrip test, the deep breathing test and the cold pressor test.

Taken together, the data by Blake et al. [4] on the change in baroreceptor sensitivity for heart rate during normal pregnancy and the puerperium are an important contribution to the literature in this field, since they give some insight into the physiological course of sympatho-vagal interaction during pregnancy at the level of the heart. This knowledge is essential for the ultimate goal in this field of autonomic research, the detection of early indicators or prognostic indices of the development of pregnancy-induced hypertension. The determination of heart rate variability represents a methodological advancement in the non-invasive study of autonomic cardiovascular control and seems to be especially suitable for studying pregnant women. For a more comprehensive assessment of autonomic circulatory control in normal and pre-eclamptic pregnancy, however, future studies are needed that combine both pre- and postsynaptic measures of sympathetic activity at rest and during various cardiovascular reflex tests.

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REFERENCES