PERSPECTIVES

Multiple oscillators in autonomic control

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It was Adrian and colleagues (Adrian *et al.* 1932) who first described the rhythmic bursting activity in mammalian sympathetic nerves that later work has shown contributes importantly to vasomotor tone. Extensive studies of this vasomotor activity have revealed several periodicities in the firing pattern: 2–6 Hz, 10 Hz, and frequencies related to the cardiac and respiratory cycles. As with other tonically active systems it is an intriguing question as to how the ongoing activity is generated and what determines its rhythmic pattern. Is it truly spontaneous or does it rely on central or peripheral afferent input? Most commonly the discharges of populations of pre- or postganglionic sympathetic neurones are synchronised into bursts locked into a 1:1 relation to the cardiac cycle, with the magnitude of the bursts waxing and waning at the period of the respiratory cycle. As a consequence the traditional view was that a population of neurones in the brainstem reticular formation randomly generated discharges, which were synchronised by powerful inputs from the arterial baroreceptors and from the respiratory system. The first important departure from this view was made by Green & Heffron (1967) and by Cohen & Gootman (1970) who subjected the discharge of vasomotor nerves to a detailed mathematical analysis, which revealed a strong 10 Hz component. This and later studies suggested that sympathetic nerve discharge was dependent on central networks inherently capable of rhythm generation. An interesting and important debate then arose (and is still ongoing) as to whether the spontaneous activity of vasomotor nerves is dependent on pacemaker cells or dedicated neural networks. There is good evidence from Guyenet's group that some neurones in vasomotor regions of the brainstem intrinsically generate activity (Sun *et al.* 1988). However, the frequency of these pacemakers is high (20 Hz) and a fast rhythm of this sort has not been observed in the discharge pattern of pre- or postganglionic sympathetic neurones. On the other hand Gebber *et al.* (1994) provided persuasive evidence for network oscillations. Using time series and spectral analysis of the relationship between the discharges in two simultaneously recorded sympathetic nerves they found that although the sympathetic activity showed a significant coherence there was a shift in the phase angle of the periodic component of the discharges in postganglionic nerves that exit from different ganglia. This suggests that the driving inputs to these outflows arise from separate pools of brainstem neurones. Subsequent studies of the discharge of brainstem neurones and simultaneous sympathetic nerve discharge confirmed the interpretation. The idea has gained further support from the studies in Gilbey's laboratory referred to in the paper by Staras *et al.* in this issue of *The Journal of Physiology*, which show that postganglionic neurones supplying the vasculature of the tail (a thermoregulatory organ) of rats exhibit a very characteristic rhythm of discharge of 0.4–1.2 Hz, which they termed the T-rhythm (Johnson & Gilbey, 1996), a rhythm that does not appear in sympathetic vasoconstrictor nerves to the kidney. Thus sympathetic vasomotor nerves supplying different vascular beds display different basic rhythms, giving rise to the idea of multiple oscillators. These patterns of rhythmic activity are likely to be representative of the basic organisation of the ventral circuits responsible for the background discharge which we term vasomotor tone and determine the level of blood pressure. These fundamental rhythms can be entrained by afferent inputs, providing the frequency of the input is close to the uncoupled frequency of the discharge, further supporting the idea that the origins of the rhythm are dependent on oscillating networks.

If the pattern of sympathetic discharge is dependent on an oscillator then it should be possible to force the oscillator to fire at the frequency of a rhythmic external input. Then a stable entrainment pattern would only occur over a narrow frequency and would be proportional to the strength of the input. This is exactly what has been observed by Gilbey's group for the T-rhythm in the discharge of vasomotor units supplying the rat tail vessels. Previous work of Gilbey's group has shown that the sympathetic activity in the tail collector nerve can be entrained by central respiratory drive, by lung inflation afferents and by aortic nerve afferents. The study by Staras *et al.* (2001) now reports experiments on the effects of somatic afferent input on the basic oscillators in this sympathetic pathway. Of course electrical stimulation of a whole bundle of afferent nerves is an artificial stimulus but it does serve as a good test of the oscillator network hypothesis. Such a study is important because it reveals where in the sympathetic pathway the afferent signal imposes its influence. It is shown that like the visceral afferent inputs somatic afferent input is at the site of rhythm generation. It is able to reset the dominant rhythm at the single oscillator level leading to a transient synchrony in the oscillator population. It is likely that this occurs in other oscillator populations of vasomotor neurones since all sympathetic cardiovascular nerves show a highly synchronised response to somatic afferent stimulation (Coote & Downman, 1966). Since this does not happen in the spinal animal where output is fractionated, decaying in strength at spinal segments remote from the input, it follows that the site of rhythm generation must be located in the brainstem. The authors argue convincingly that co-ordinated responses in the sympathetic outflow depend on a resetting of multiple sympathetic oscillators.

How important might this be to the function of the sympathetic nervous system? The leading idea, of how oscillating networks generating 'spontaneous' activity may be useful to the sympathetic control system, holds that the linking of synchronised oscillations provides a signal that adjusts the strength of ganglionic synapses. Furthermore we know that throughout the vascular beds there is an optimum frequency of post-ganglionic activity for effective activation. The resetting of multiple oscillators is a way of ensuring this optimum patterning of discharge is attained.

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