Chapter 4
PATHOPHYSIOLOGICAL ALTERATIONS OF SYMPATHOVAGAL BALANCE

Tools which are more adequate to explore pathophysiology are not necessarily the most suitable ones to interpret physiology. In this Chapter, among other issues, the usefulness of applying both the concept of sympathovagal balance and its frequency domain assessment to the study of pathophysiological mechanisms will be analyzed. Numerous limitations will emerge, together with evident advantages. However, some initial considerations on the characteristics of a tool capable of exploring abnormalities in cardiovascular neural regulation might be appropriate.

Requirements for a tool

What is required is the capability of detecting alterations that may vary from the most drastic to only slight ones, yet crucial to interpret the ongoing pathophysiological process. Thus, it is no surprise that an adequate methodology is of paramount importance. In addition, some uncertainty is also intrinsic in the matter under scrutiny. To take an example, a continuous electrocardiographic recording from a normal subject under resting conditions, especially when analyzed with a time-frequency spectral methodology (Jasson et al. 1997; Furlan et al. 1998b), displays continuous oscillations in amplitude and frequency of spectral components: it is a common laboratory experience that sudden emotionally charged thinking during the recording is capable of markedly altering the spectral profile. Hence the sensitivity of this approach to changes that would presumably be undetectable by any other currently available technique, also represents a possible shortcoming for clinical studies.

Yet, under well controlled laboratory conditions the short and long-term reproducibility of frequency domain measurements
appeared to be consistent, especially when a stimulus like head-up tilting was used in order to shift the sympathovagal balance (Pagani et al. 1986b; Pitzalis et al. 1996).

Ageing (Pagani et al. 1986b; Lipsitz et al. 1990; Montano et al. 1994) and gender differences (Huikuri et al. 1996a; Barnett et al. 1999; Fagard et al. 1999) should also be taken into careful account. Ageing, although it produces a progressive reduction of variance and hence of spectral components in absolute units, does not modify the LF/HF ratio (Pagani et al. 1986b). This suggests that a dynamic equilibrium between the modulatory influences exerted by the two branches of the autonomic nervous system exists at all ages (Fagard et al. 1999), a phenomenon that can hardly be appreciated by measuring an isolated output. Interestingly, heritable factors (Singh et al. 1999) seem to explain a substantial proportion of HRV that, therefore, should not be purely ascribed to environmental factors.

However, what has to be emphasized and has always been stressed by the promoters of this approach, is that power spectrum analysis of HRV does not provide measurements of sympathetic and vagal activities, but only markers of sympathetic and vagal modulations and of their interaction (Malliani et al. 1991a; Malik and Camm 1993; Task Force 1996). This crucial point is often forgotten by neophytes and repeatedly discovered by detractors (Eckberg 1997; Grassi and Esler 1999).

Moreover, an adequate responsiveness of cardiovascular targets, and in particular of sinus node activity, to neural modulation needs to be present in order to apply spectral methodology to the assessment of sympathovagal balance. Thus, conditions like congestive heart failure, characterized by an increased concentration of circulating catecholamines and \( \beta_1 \) adrenergic receptor down-regulation (Packer 1998), can only provide quite complex results, as reported subsequently. On the other hand, the disappearance of an LF component in the HRV of patients with congestive heart failure (Guzzetti et al. 1995) or after myocardial infarction (Lombardi et al. 1987) is likely to indicate a diminished responsiveness of the target organ to sympathetic modulation (Malliani et al. 1994a; Lombardi 1999) and to have an ominous prognostic value.

Obviously in research we can plan to measure only what can be measured under various conditions and, on the whole, it is likely that complementary information is provided by multifarious approaches. However in this very perspective it is difficult to accept