the activity level from periods of enforced rest to periods of scripted activity (3). Finally, we could generate similar SDANN values by dual-chamber pacing whether driven by sinus node activity or by a mechanical activity sensor (4). Taken together, these findings indicate the major role of activity in inducing SDANN.

Fantoni et al. found that the increases in SDANN were parallel to improvements in functional capacity, and Adamson et al. (5) reported that a decline in physical activity corresponded with a decrease in SDANN prior to a clinical deterioration.

We propose that patients with successful CRT experience hemodynamic improvements, an improvement in functional capacity, and an increase in physical activity with the resultant modulation of heart rate, which is reflected by an increase in SDANN. Finally, none of this diminishes the importance of SDANN, but does suggest that its important role may not involve the autonomic nervous system.

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# REPLY

We appreciate the important comments made by Sheldon et al. who questioned our interpretation (1) that changes in the standard deviation of the averages of intrinsic intervals in the 288 5-minute segments of a day (SDANN) could reflect changes in autonomic interactions on the heart. The criticism was based on the observation—provided by their own laboratory—that SDANN is "possibly and partly" affected by physical activity. We regret to have overlooked their work (2), which showed that increased level of physical activity is a possible source of the observed increase in 24-h SDANN; yet this does not imply at all that SDANN is not an index of autonomic modulation of the heart.

Although our understanding of the physiological background of long-term, in comparison with short-term, heart rate variability (HRV) is more incomplete, there is ample evidence that the autonomic nervous system also plays a major role in the generation of long-term HRV. Indeed, parasympathetic blockade with atropine decreases 24-h HRV at all frequencies (3); after heart transplantation, long-term HRV is reduced at all frequencies (4), and long-term HRV is also depressed in the autonomic neuropathy occurring in diabetic patients (5).

Though short-term time-domain HRV is substantially dependent on respiratory arrhythmia and fast baroreflex regulation, long-term measures have been regarded as reflecting the response of cardiac regulation to challenges of daily life. Several factors have been invoked to explain some limitations in the correlation between short- and long-term HRV, including slower fluctuations due to baroreflexes, neurohormonal rhythms and circadian patterns, differences between day and night, and both physical and mental activity.

The role of a deranged baroreflex in affecting autonomic outflow to the heart is firmly established. For example, a reduced left ventricular function depresses baroreflex sensitivity and reduces SDNN (6). The hemodynamic improvement brought about by cardiac resynchronization therapy restores cardiac contractility, which results in an improvement in baroreceptor activity and in long-term HRV. Whereas we cannot exclude that an increase in physical activity might have contributed to the observed improvement in long-term HRV, we believe that the autonomic nervous system is the primary determinant of HRV in both the short and long term.

In conclusion, we do not entirely share the view by Sheldon and colleagues that the role of SDNN does not involve the autonomic nervous system.

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