Comparing resting skin sympathetic nerve activity between groups: caution needed

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TO THE EDITOR: We read with interest the recently published work of Park et al. (10) examining differential regional control of sympathetic nerve activity in end-stage renal disease (ESRD). These investigators compared integrated multiunit recordings of muscle sympathetic nerve activity (MSNA) and skin sympathetic nerve activity (SSNA) at rest between patients with ESRD and healthy age- and gender-matched control subjects, using the technique of microneurography. Similar to previous reports, the ESRD patients demonstrated greater resting MSNA compared with controls. However, SSNA was similar between the two groups, leading the authors to conclude that “…although sympathetic activity directed to muscle is significantly elevated, activity directed to skin is not elevated in ESRD.” Although we commend the authors for addressing this important issue, there are major limitations in comparing basal SSNA between groups that should be considered, despite the work of others who have performed similar analyses (5, 8, 11).

The activity of multiunit SSNA recordings is comprised of vasoconstrictor, sudomotor, pilo erector, and possibly active vasodilator fibers (1, 4, 7). Importantly, SSNA bursts occur in seemingly random fashion as bursts of irregular shape and duration, making inter-recording quantification difficult and limited. In contrast, measurements of MSNA are dominated primarily by sympathetic vasoconstrictor impulses, with the burst pattern occurring in a pulse synchronous fashion due to tight regulation by the arterial baroreflex (2, 3). Because of the pulse synchronicity of MSNA, only a single burst will occur during a given cardiac cycle, and therefore the quantification of burst frequency (i.e., bursts/min) is relatively easy. On the other hand, SSNA bursts occur with no apparent rhythmicity. Moreover, as shown in Fig.1, SSNA bursts occur in varying widths, with some bursts demonstrating multiple peaks. In this case, does a multiple peak burst represent one or more bursts? Indeed, we are unaware of any study that has reported on the reproducibility of SSNA, whereas MSNA burst frequency is highly reproducible from day to day, even when recordings have been separated by 21 mo (12). Importantly, the variations in SSNA burst shapes reflect either an increased number of efferent neurons firing and/or multiple firing of the same neuron, the impact of which is discounted by simply counting the number of bursts. An alternative approach would be to quantify total SSNA activity, as measured by area under the curve. However, while this is appropriate for comparison within a subject (as long as the microelectrode position has not changed), it cannot be used to compare responses between subjects, as SSNA burst area is largely affected by the position of the microelectrode within the nerve fascicle, which is unknown. Therefore, unlike MSNA, defining “basal” SSNA to compare groups is not practical.

Furthermore, as originally discussed by Wallin and colleagues (1, 7), because multiunit SSNA recordings are comprised of a mixture of various types of fibers, it is highly unlikely that there is a specific intrafascicular site from which the activity of only one type of fiber can be recorded using microneurography. This point is corroborated by histological evidence demonstrating that individual C fiber axons constantly interchange between Schwann cells, creating a complex system of fibers within a given cell (9). The relative inability to control for the fiber composition of SSNA recordings makes the comparison of multiunit recordings between subjects unfeasible. For example, it is possible to surmise that similar SSNA between subjects could be achieved by differing activity of efferent neurons: subject A could have high vasoconstrictor and low sudomotor neural activity, while subject B may have low vasoconstrictor and high sudomotor activity. Moreover, within a subject, the fiber composition of a SSNA recording may differ simply on the location of the microelectrode within the nerve fascicle, as the recording is determined by the proximity of the electrode to respective neural fibers (i.e., vasoconstrictor, sudomotor, etc).

The determination of differential sympathetic outflow amid different vascular beds is an important question that Park et al. (10) and others (5, 8, 11) have attempted to address by measuring multiunit SSNA using standard microneurographic techniques. However, considering the potential for multiple fiber types in SSNA recordings and the irregular nature of SSNA bursts, we feel that comparison of SSNA burst frequency between subjects and furthermore among groups is impractical. While SSNA is entirely appropriate to assess sympathetic reactivity to a given stimulus within a subject on a particular day, readers should be aware of the limitations of quantifying SSNA measurements between groups.

REFERENCES


Fig. 1. Segment of an original resting skin sympathetic nerve activity (SSNA) recording from a healthy subject demonstrating bursts of irregular shapes and sizes, with some bursts displaying multiple peaks (arrows). This makes the determination of the onset and end of the SSNA burst difficult. Also, by simply counting the number of bursts, the impact of burst width (i.e., more neurons firing and/or multiple firing of the same neuron) is ignored.