

## Absence of arterial baroreflex modulation of skin sympathetic activity and sweat rate during whole-body heating in humans

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1. Prior findings suggest that baroreflexes are capable of modulating skin blood flow, but the effects of baroreceptor loading/unloading on sweating are less clear. Therefore, this project tested the hypothesis that pharmacologically induced alterations in arterial blood pressure in heated humans would lead to baroreflex-mediated changes in both skin sympathetic nerve activity (SSNA) and sweat rate.
2. In seven subjects mean arterial blood pressure was lowered ( $\sim 8$  mmHg) and then raised ( $\sim 13$  mmHg) by bolus injections of sodium nitroprusside and phenylephrine, respectively. Moreover, in a separate protocol, arterial blood pressure was reduced via steady-state administration of sodium nitroprusside. In both normothermia and heat-stress conditions the following responses were monitored: sublingual and mean skin temperatures, heart rate, beat-by-beat blood pressure, skin blood flow (laser-Doppler flowmetry), local sweat rate and SSNA (microneurography from peroneal nerve).
3. Whole-body heating increased skin and sublingual temperatures, heart rate, cutaneous blood flow, sweat rate and SSNA, but did not change arterial blood pressure. Heart rate was significantly elevated (from  $74 \pm 3$  to  $92 \pm 4$  beats  $\text{min}^{-1}$ ;  $P < 0.001$ ) during bolus sodium nitroprusside-induced reductions in blood pressure, and significantly reduced (from  $92 \pm 4$  to  $68 \pm 4$  beats  $\text{min}^{-1}$ ;  $P < 0.001$ ) during bolus phenylephrine-induced elevations in blood pressure, thereby demonstrating normal baroreflex function in these subjects.
4. Neither SSNA nor sweat rate was altered by rapid (bolus infusion) or sustained (steady-state infusion) changes in blood pressure regardless of the thermal condition.
5. These data suggest that SSNA and sweat rate are not modulated by arterial baroreflexes in normothermic or moderately heated individuals.

Skin sympathetic nerve activity (SSNA) contains neural signals of sudomotor and vasomotor origins (Vallbo *et al.* 1979; Janig & Kummel, 1981). A number of factors (e.g. mental stress, exercise and hyperventilation) alter SSNA (Delius *et al.* 1972*b*; Hagbarth *et al.* 1972). SSNA is also very responsive to changes in internal as well as skin temperatures (Bini *et al.* 1980; Vissing, 2000). Cooling presumably increases the vasoconstrictor component of the SSNA signal, while thermoneutral conditions or slight heating withdraws this activity. Upon more pronounced heating, SSNA increases dramatically, which is thought to be the neural signal responsible for increasing sudomotor and/or cutaneous active vasodilator activities.

The effects of baroreceptor loading/unloading on SSNA do not consistently agree with published reports of

baroreceptor modulation of skin blood flow. In normothermic individuals, direct stimulation of the carotid sinus nerve (Wallin *et al.* 1975), Valsalva manoeuvres (Delius *et al.* 1972*b*), lower-body negative pressure (LBNP; Vissing *et al.* 1994), or spontaneous variations in blood pressure (Hagbarth *et al.* 1972) fail to alter SSNA. These data suggest that the vasoconstrictor limb of SSNA is not altered by baroreflexes in normothermia. These findings are perplexing given data from our and others' laboratories demonstrating that baroreceptor unloading in normothermic subjects decreases cutaneous vascular conductance (Johnson *et al.* 1973; Rowell *et al.* 1973; Tripathi & Nadel, 1986; Kellogg *et al.* 1990; Crandall *et al.* 1996). Given that sudomotor, pilomotor and active vasodilator activity is presumably absent in the SSNA recording when the individual is in normothermia (in the

absence of arousal stimuli) coupled with the aforementioned lack of change in SSNA during baroreceptor perturbations in normothermic individuals, the neural signal leading to decreases in cutaneous vascular conductance during baroreceptor unloading remains unknown.

Whole-body heating causes pronounced increases in SSNA. It is presumed that this increase in SSNA leads to increases in sweating and/or skin blood flow (Hagbarth *et al.* 1972; Normell & Wallin, 1974). The effects of baroreceptor loading/unloading on SSNA in heated individuals are not clear. Dodt *et al.* (1995) reported that SSNA decreases in mildly heated individuals during baroreceptor unloading with LBNP and with head-up tilt, and others have reported that SSNA displays cardiac rhythmicity (Bini *et al.* 1981; Macefield & Wallin, 1996). Taken together, these studies imply that baroreceptors are capable of modulating SSNA. In contrast, Vissing *et al.* (1994) suggested that decreases in SSNA during LBNP in mildly heated individuals were due to skin-surface cooling associated with LBNP and not due to baroreceptor unloading. These conflicting findings are further clouded by observations that baroreceptor unloading in heated subjects have been reported to decrease cutaneous vascular conductance via withdrawal of cutaneous active vasodilatation (Kellogg *et al.* 1990; Crandall *et al.* 1996), decrease sweat rate (Mack *et al.* 1995), as well as decrease the slope relating the elevation of sweat rate to the elevation in internal temperature (Solack *et al.* 1985). Taken together, the effects of baroreflex modulation of SSNA, and accompanying end-organ responses, in normothermic and heat-stressed individuals remain an open question.

A limitation of the aforementioned studies is the potentially confounding effects of non-baroreflex-mediated responses (e.g. emotional responses or skin-surface cooling) affecting SSNA during the perturbation used to change blood pressure. An alternative method of baroreceptor loading/unloading is the use of pharmacological agents to decrease and increase blood pressure. This method alters arterial blood pressure without causing skin-surface cooling or emotional responses that may accompany other methods of baroreceptor loading/unloading such as LBNP. Prior investigations have used these methods to assess baroreflex control of muscle sympathetic nerve activity under a variety of conditions (Rudas *et al.* 1999). To the authors' knowledge no study has combined the effects of whole-body heating with pharmacologically induced arterial baroreceptor modulation with a goal of investigating baroreflex control of SSNA and sweating. Such a study may be beneficial in furthering an understanding of baroreflex control of SSNA and sweat rate in heat-stressed individuals. Therefore, the purpose of this project was to test the hypothesis that arterial baroreflexes modulate SSNA and sweat rate during pharmacological manipulations of blood pressure in normothermic and heat-stressed humans.

## METHODS

### Subjects

Seven healthy subjects (3 men, 4 women) participated in the project. The participants' mean age was  $27.7 \pm 2.1$  years and all were of typical height ( $174.5 \pm 2.7$  cm), weight ( $69.9 \pm 2.4$  kg), and body surface area ( $1.40 \pm 0.1$  m<sup>2</sup>; Du Bois & Du Bois, 1916). Written informed consent was obtained from all participants prior to enrolling in this study. The protocol and informed consent received institutional approval and the study conformed to the Declaration of Helsinki.

### Measurements

Multiunit postganglionic SSNA was recorded from the common peroneal nerve. After mapping the nerve pathway via external stimulation, an uninsulated reference electrode was inserted 2–3 cm from the projected insertion site of the recording electrode. A second recording electrode, with a tip diameter between 1 and 5  $\mu$ m, was inserted into the peroneal nerve dorsal to the fibular head. The signal was amplified  $\times 1000$  and passed through a band-pass filter (700–2000 Hz) with a gain between 60 and 90 (Iowa Bioengineering, Iowa City, IA, USA). The filtered neurogram was then rectified and integrated to obtain a mean voltage display. This signal was sampled at 200 Hz via a computer data acquisition system (Biopac Systems, Santa Barbara, CA, USA). Identification of SSNA was determined following standard guidelines previously published (Delius *et al.* 1972*a,b*). Total activity of multiunit skin sympathetic nerves was obtained with the aid of data analysis software *post hoc* (Acknowledge, Biopac Systems). Heart rate was obtained from an electrocardiogram (SpaceLabs, Redmond, WA, USA) with the signal interfaced with a cardi tachometer (CWE, Ardmore, PA, USA). Arterial blood pressure was obtained on a beat-by-beat basis via a tonometric blood pressure system (Collins, San Antonio, TX, USA). Local skin blood flow was measured via laser-Doppler flowmetry using integrating flow probes (Perimed, North Rayalton, OH, USA) attached to the dorsal portion of the foot within the area of peroneal nerve innervation. Cutaneous vascular conductance (CVC) was indexed by dividing laser-Doppler flux values by mean arterial blood pressure (MAP) and multiplying that number by 100. Sweat rate was measured via capacitance hygrometry (Viasala, Woburn, MA, USA) by perfusing 100% nitrogen at a flow rate of 300 ml min<sup>-1</sup> through a ventilated capsule (surface area = 2.83 cm<sup>2</sup>) attached to the skin also within the area of innervation of the nerve fascicle being recorded. Internal temperature ( $T_{si}$ ) was indexed from a thermocouple placed in the sublingual sulcus. Mean skin temperature ( $T_{sk}$ ) was measured via the weighted average of six thermocouples attached to the skin (Taylor *et al.* 1989).

### Protocols

The protocol consisted of performing the outlined procedures first under normothermic conditions, followed by repeating the procedures after whole-body heating. Whole-body heating was performed via perfusing 46°C water through a tube-lined suit worn by each subject (Carleton Technologies, Tampa Bay, FL, USA). This method of heating typically increases skin temperature to  $\sim 38^\circ\text{C}$  and  $T_{si}$  0.6–1.0°C after 30–60 min of heating. In the present protocol water temperature perfusing the suit was slightly reduced to 44–45°C 10–15 min prior to drug infusion in an attempt to cause  $T_{si}$  to plateau during the ensuing baroreceptor perturbations.

### Bolus injections of nitroprusside and phenylephrine

In both thermal conditions blood pressure was first decreased then increased via bolus infusions of 100  $\mu$ g sodium nitroprusside followed by 150  $\mu$ g phenylephrine, respectively. Care was taken to avoid arousing the subject during drug infusion. This was accomplished by having the subject close his/her eyes 30–60 s prior to intravenous

**Table 1. Effects of whole-body heating on temperature and haemodynamic responses**

Variable	Normothermia	Whole-body heating	<i>P</i> value
MAP (mmHg)	76 ± 2	76 ± 2	0.73
HR (beats min <sup>-1</sup> )	55 ± 3	74 ± 3	< 0.001
CVC (units)	17 ± 2	115 ± 15	0.001
SR (mg cm <sup>-2</sup> min <sup>-1</sup> )	0.17 ± 0.08	0.69 ± 0.12	0.005
<i>T</i> <sub>sl</sub> (°C)	36.8 ± 0.1	37.4 ± 0.1	0.004
Mean <i>T</i> <sub>sk</sub> (°C)	34.7 ± 0.05	37.9 ± 0.3	< 0.001

MAP, mean arterial pressure; HR, heart rate; CVC, cutaneous vascular conductance; SR, sweat rate; *T*<sub>sl</sub>, sublingual temperature; mean *T*<sub>sk</sub>, mean skin temperature. Values are expressed as means ± S.E.M.

drug administration, and by the investigators using visual cues to communicate the onset of drug delivery. Thus, the subject was unaware of the onset of drug delivery thereby minimizing any anticipatory response associated with drug delivery. Bolus phenylephrine infusion began approximately 60 s after the onset of the nitroprusside infusion. In each thermal condition three of these challenges were performed, with the responses within each thermal condition averaged. This method of pharmacological manipulation of blood pressure to assess baroreflex control of muscle sympathetic nerve activity and heart rate has been described previously (Ebert & Cowley, 1992; Rudas *et al.* 1999).

#### Steady-state infusions of sodium nitroprusside

In a separate protocol, four subjects received steady-state intravenous infusions of sodium nitroprusside that were administered over 8–10 min in both the normothermic and heat-stress conditions. Doses of nitroprusside (20–100 µg min<sup>-1</sup>) were sequentially infused via a constant infusion pump through the venous catheter. This method of sodium nitroprusside administration causes sustained decreases in MAP leading to baroreflex-mediated increases in heart rate over the duration of the infusion (Birkett *et al.* 1992).

#### Data analysis

Data were continuously acquired throughout normothermic and heat-stress procedures. For the bolus procedure, data were averaged into the following 20 s blocks: immediately prior to nitroprusside infusion, immediately prior to phenylephrine infusion, and 10 s prior to and after the highest stable blood pressure achieved with phenylephrine infusion, which typically occurred between 40 and 60 s after phenylephrine administration. Data analysis was limited to 20 s periods due to the method used to alter blood pressure (i.e. sequential bolus infusions) in combination with the short action of the drugs. The goal of this method of data analysis was to obtain data when blood pressure was at its lowest point during nitroprusside infusion and at its highest point during phenylephrine infusion. For the steady-state protocol, data were averaged from the minute immediately prior to the onset of drug delivery and from the last minute of each dose of nitroprusside. For both thermal conditions, SSNA was normalized based upon the 20 s period (for bolus protocol) and the 1 min period (for steady-state protocol) immediately prior to each drug infusion. This method of analysis eliminates potential errors associated with subtle changes in electrode position that may occur over long duration SSNA recordings.

In each thermal condition, data (i.e. heart rate, MAP, sweat rate and SSNA) were analysed via one-way repeated analysis of variance to identify differences between pre-drug, sodium nitroprusside and phenylephrine phases. Assessment of the effects of whole-body heating on temperature and haemodynamic responses was undertaken with Student's paired *t* test. No direct statistical

comparisons were performed for SSNA between normothermic and heat-stress conditions due to subtle shifts in the electrode during the course of whole-body heating requiring repositioning of the electrode for some subjects. Skin blood flow was not analysed during the drug perturbations due to the confounding effects of the drug acting directly on the cutaneous vasculature independent of neural control. All values are reported as means ± S.E.M. The  $\alpha$ -level for all statistical analyses was set at 0.05.

## RESULTS

#### Temperature and cardiovascular variables

Whole-body heating increased *T*<sub>sk</sub> to 37.9 ± 0.3°C, while *T*<sub>sl</sub> increased approximately 0.6°C and CVC increased more than 6-fold when compared to normothermia (see Table 1). Cardiovascular variables in normothermic and heat-stress conditions are listed in Table 1. Baseline MAP was maintained during the heat stress while heart rate increased significantly when compared to normothermia. In normothermia, baseline MAP was 76 ± 2 mmHg, and decreased with bolus sodium nitroprusside to 65 ± 2 mmHg (*P* < 0.05), followed by an increase to 79 ± 2 mmHg (*P* < 0.05 from baseline) with infusion of phenylephrine (see Table 2). Comparable MAP values were obtained during hyperthermia (baseline: 76 ± 2 mmHg; nitroprusside: 69 ± 3 mmHg (*P* < 0.05 from baseline); phenylephrine: 82 ± 2 mmHg (*P* < 0.05 from baseline)). Prior to drug administration, heart rate was 55 ± 3 and 74 ± 3 beats min<sup>-1</sup> for normothermic and heat-stress conditions, respectively. Sodium nitroprusside infusion resulted in an increase in heart rate to 72 ± 4 and 92 ± 4 beats min<sup>-1</sup> (both *P* < 0.05 from respective baselines), while phenylephrine infusion resulted in a decrease in heart rate to 51 ± 3 and 68 ± 4 beats min<sup>-1</sup> (both *P* > 0.05 from respective baselines) for normothermic and heat-stress conditions, respectively.

Steady-state infusion of nitroprusside at the highest dose received by all subjects (60 µg min<sup>-1</sup>) significantly decreased MAP in both thermal conditions (normothermia: from 76 ± 3 to 68 ± 2 mmHg; heat stress: from 75 ± 1 to 63 ± 1 mmHg; both *P* < 0.05), resulting in baroreflex-mediated increases in heart rate (normothermia: from 61 ± 2 to 83 ± 5 beats min<sup>-1</sup>; heat stress: from 85 ± 4 to 103 ± 5 beats min<sup>-1</sup>; both *P* < 0.05; see Table 3).

**Table 2. Effects of baroreceptor loading/unloading via bolus infusions of sodium nitroprusside (NP) and phenylephrine (PE) on sweat rate, mean arterial blood pressure (MAP) and heart rate during normothermia and whole-body heating**

Drug	Sweat rate ( $\text{mg cm}^{-2} \text{min}^{-1}$ )	MAP (mmHg)	Heart rate (beats $\text{min}^{-1}$ )
Normothermia			
Baseline	$0.17 \pm 0.03$	$76 \pm 2$	$55 \pm 3$
NP	$0.18 \pm 0.04$	$65 \pm 2^*$	$72 \pm 4^*$
PE	$0.20 \pm 0.04$	$79 \pm 2^*$	$51 \pm 3$
Whole-body heating			
Baseline	$0.69 \pm 0.12$	$76 \pm 2$	$74 \pm 3$
NP	$0.72 \pm 0.12^*$	$69 \pm 3^*$	$92 \pm 4^*$
PE	$0.74 \pm 0.12^*$	$82 \pm 2^*$	$68 \pm 3$

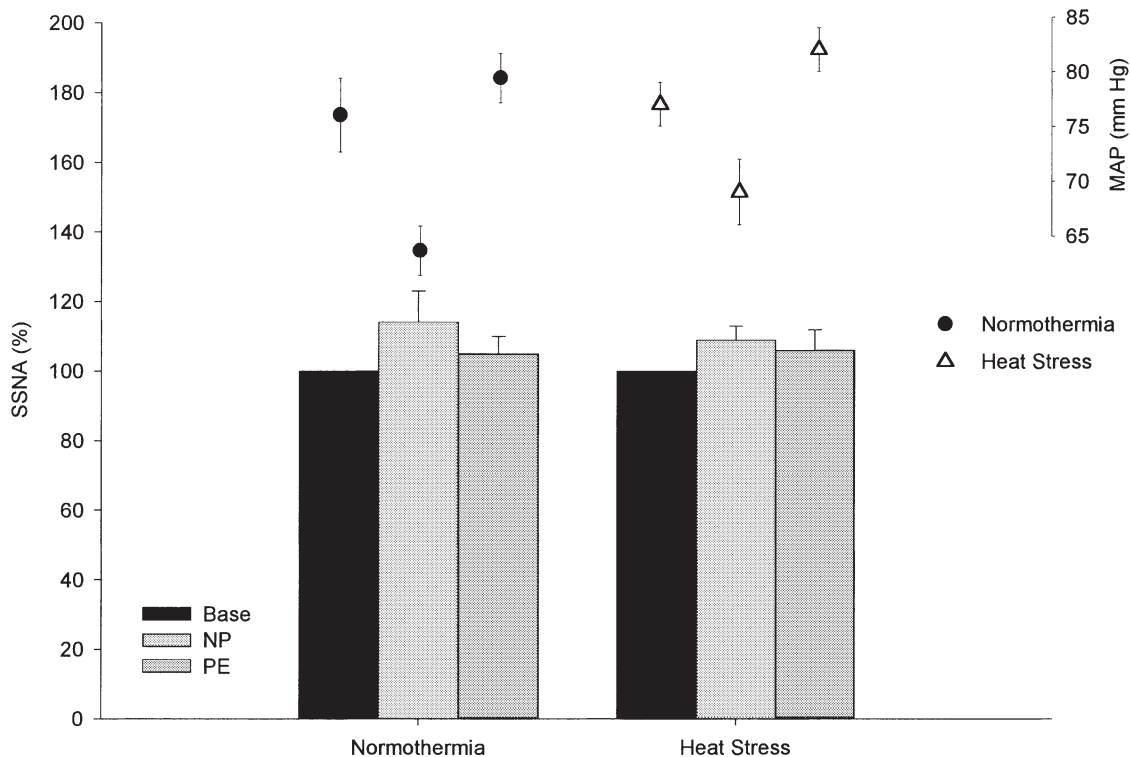
Values are expressed as means  $\pm$  S.E.M. \*Significant difference from baseline (i.e. pre-drug) conditions.

### Sweat rate and SSNA

SSNA was not significantly altered during decreases or increases in arterial blood pressure via bolus infusions, regardless of the thermal status (see Fig. 1). As MAP was reduced, SSNA did not decrease; if anything there was a small, but statistically insignificant, increase in skin nerve traffic in both thermal conditions (see Fig. 1). An example of the time course of pharmacologically induced changes in MAP, heart rate and subsequent lack of an

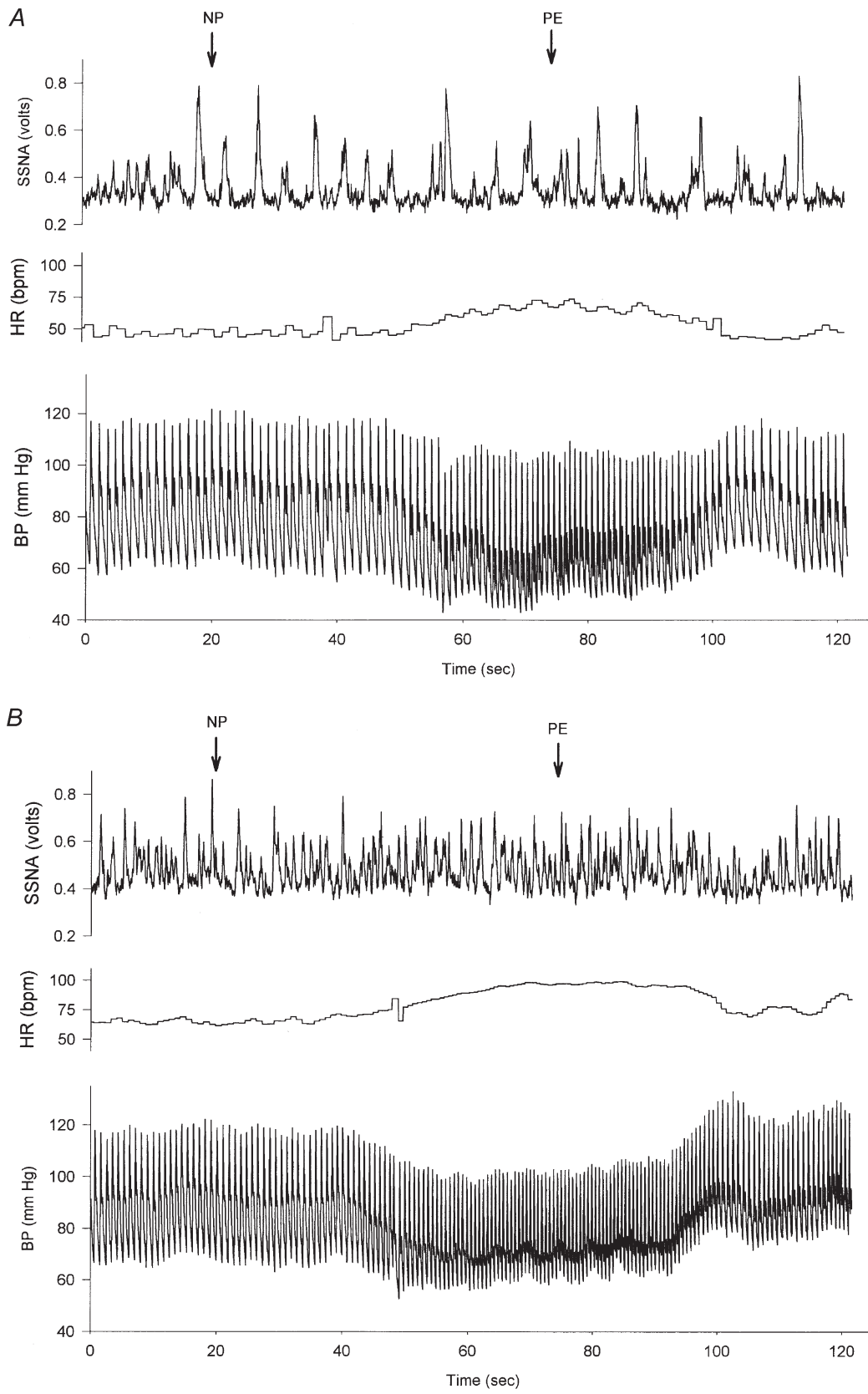
effect on SSNA can be seen in Fig. 2A for normothermia and in Fig. 2B for heat-stress conditions. The subject in Fig. 2 clearly increased SSNA in the heat-stress condition when compared to normothermia. The pronounced elevation in SSNA that occurred during the heat stress rapidly decreased during cooling following the end of the heat stress (see Fig. 3).

For the bolus infusion protocol, sweat rate increased to a mean value of  $0.69 \pm 0.12 \text{ mg cm}^{-2} \text{ min}^{-1}$  prior to drug



**Figure 1. Effects of baroreceptor modulation via bolus sodium nitroprusside (NP) and phenylephrine (PE) administration on mean arterial blood pressure (MAP) and normalized skin sympathetic nerve activity (SSNA) during both normothermia and hyperthermia**

Baseline (Base) prior to each thermal condition was used for normalization (i.e. 100%). Regardless of the thermal conditions, SSNA was unaffected by baroreceptor unloading or loading. Values are expressed as means  $\pm$  S.E.M.



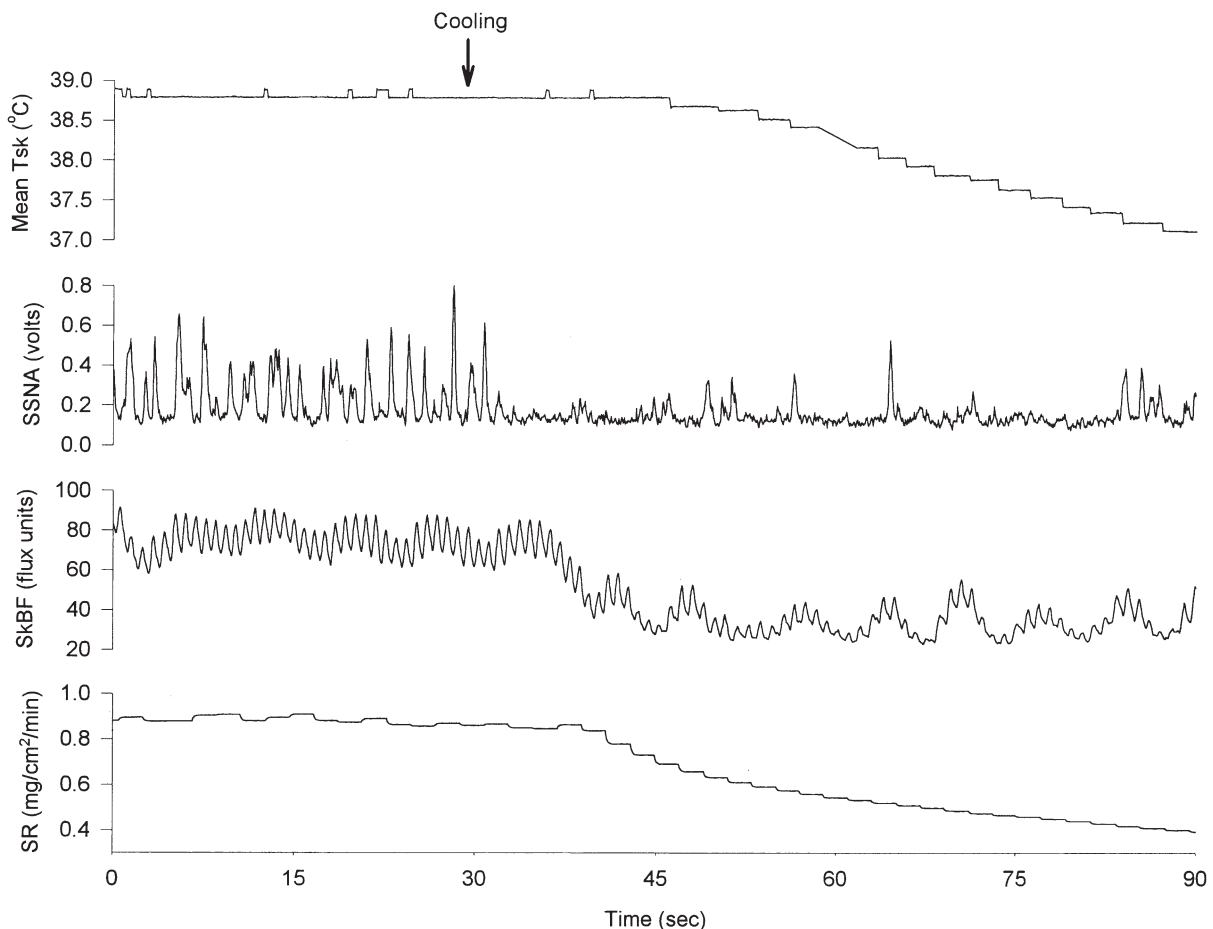
**Figure 2**

Representative data from one subject during bolus sodium nitroprusside (NP) and phenylephrine (PE) infusions on skin sympathetic nerve activity (SSNA), heart rate (HR), and arterial blood pressure (BP) during normothermia (A) and during heat stress (B).

**Table 3. Effects of steady-state infusions of sodium nitroprusside (NP) on mean arterial pressure (MAP), heart rate, normalized skin sympathetic nerve activity (SSNA) and sweat rate (SR) during both thermal conditions**

Dose of NP ( $\mu\text{g min}^{-1}$ )	MAP (mmHg)	Heart rate (beats $\text{min}^{-1}$ )	SR ( $\text{mg cm}^{-2} \text{min}^{-1}$ )	SSNA (% baseline)
Normothermia				
Baseline	$76 \pm 3$	$61 \pm 2$	$0.14 \pm 0.04$	$100 \pm 0$
NP 20	$74 \pm 3$	$65 \pm 5$	$0.12 \pm 0.02$	$99 \pm 5$
NP 40	$70 \pm 1^*$	$76 \pm 6^{*\dagger}$	$0.16 \pm 0.04$	$99 \pm 8$
NP 60	$68 \pm 2^{*\dagger}$	$83 \pm 5^{*\dagger\ddagger}$	$0.18 \pm 0.07$	$96 \pm 7$
Whole-body heating				
Baseline	$75 \pm 1$	$85 \pm 4$	$0.87 \pm 0.18$	$100 \pm 0$
NP 20	$70 \pm 3$	$88 \pm 4$	$0.88 \pm 0.18$	$101 \pm 2$
NP 40	$69 \pm 1$	$98 \pm 4^{*\dagger}$	$0.88 \pm 0.17$	$103 \pm 4$
NP 60	$63 \pm 1^{*\dagger\ddagger}$	$103 \pm 5^{*\dagger\ddagger}$	$0.89 \pm 0.17$	$101 \pm 3$

The cited doses of nitroprusside (20, 40 and 60  $\mu\text{g min}^{-1}$ ) represent the doses that every subject received over a period of 8–10 min. Two subjects received higher doses (80 and 100 NP  $\mu\text{g min}^{-1}$ ), and no changes in SSNA or sweat rate were observed at these higher doses (data not shown). Values are expressed as means  $\pm$  S.E.M. \*Significant difference from baseline (i.e. pre-drug) conditions; †significant difference from NP 20; ‡significant difference from NP 40.



**Figure 3**

Representative data from one subject during whole-body cooling after the heat stress on mean skin temperature ( $T_{\text{sk}}$ ), skin sympathetic nerve activity (SSNA), skin blood flow (SkBF) and sweat rate (SR). Sublingual temperature was not altered during the period represented by this figure.

administration during the heat stress. Decreases in MAP with bolus injections of sodium nitroprusside did not significantly reduce sweat rate. In contrast, there was a small, but statistically significant, increase in sweat rate when MAP was reduced (see Table 2). This increase in sweat rate persisted during phenylephrine infusion, but no differences in sweat rate were identified between the nitroprusside and phenylephrine conditions. We do not believe this small increase in sweat rate was due to unloading or loading of arterial baroreceptors. Rather, we believe that this slight increase in sweat rate was due to small, progressive and statistically significant increases in  $T_{\text{sk}}$  (0.03 °C) during the period in which drugs were administered, despite attempts to cause  $T_{\text{sk}}$  to plateau prior to drug administration. Nevertheless, sweat rate did not decrease when MAP was reduced as would be expected if sweat rate was modulated by baroreceptors.

Similar to that observed during the bolus infusion protocol, sustained reductions in arterial blood pressure over 8–10 min via steady-state infusions of sodium nitroprusside also did not elicit significant changes in SSNA or sweat rate regardless of the thermal condition (see Table 3).

## DISCUSSION

The major findings of the present study are that arterial blood pressure modulation, caused by bolus sodium nitroprusside and phenylephrine infusions, as well as by steady-state nitroprusside infusions, failed to alter either SSNA or sweat rate. This observation was consistent in both normothermic and heat-stress conditions. These data provide evidence demonstrating that SSNA and sweating may not be modulated by arterial baroreceptors even when SSNA and sweating rate are elevated during whole-body heating. The unique aspects of this study include the method of blood pressure modulation, the degree of heat stress, and simultaneous recording of both SSNA and end-organ responses (e.g. sweat rate) during blood pressure challenges.

Whole-body heating did not alter baseline MAP (see Tables 1 and 3). Prior studies indicate that whole-body heating decreases central venous pressure by 3–5 mmHg (Rowell, 1983; Crandall *et al.* 1999). Maintenance of MAP, despite decreases in central venous pressure, is accomplished by increasing cardiac output and by altering regional vascular resistances (Johnson & Proppe, 1996). In the present study, baseline heart rate increased  $\sim 19$  beats  $\text{min}^{-1}$  and cutaneous vascular conductance increased over 6-fold with the heat stress (see Table 1).

Bolus injections of sodium nitroprusside decreased blood pressure while phenylephrine increased blood pressure from the nitroprusside nadir. In all cases phenylephrine either returned blood pressure to pre-drug levels or increased it 3–4 mmHg above this level. Changes in arterial blood pressure as a result of these drugs were

similar in both thermal conditions. However, the magnitude of reduction in arterial blood pressure during the heat stress with sodium nitroprusside was slightly less than that observed in normothermia (see Fig. 1). In prior studies, sodium nitroprusside and phenylephrine bolus injections with identical doses resulted in slightly greater changes in blood pressure than that seen in this study (Ebert & Cowley, 1992). Even though arterial blood pressure was not altered to the same extent as in previous work, we are confident that blood pressure changed sufficiently to evoke baroreflex-mediated responses given the observed change in heart rate (see Fig. 2 and Tables 2 and 3).

We hypothesized that baroreceptor modulation, as previously shown by Mack *et al.* (1995), would decrease sweat rate during the heat stress in an effort to preserve hydration status. This, however, was not observed in the present study, as sweat rates were not altered despite rapid and sustained reductions in MAP induced with sodium nitroprusside. However, three important distinctions should be raised between the present investigation and previous studies with respect to sweat rate and baroreceptor unloading. First, we used water-perfused suits to increase internal temperature while Mack *et al.* (1995) used dynamic exercise in a moderately warm room to heat the subjects. Thus, differing stimuli to increase internal temperature or exercise itself may result in conflicting findings. Secondly, Mack *et al.* (1995) and Solack *et al.* (1985) used LBNP to unload baroreceptors, which may cause skin-surface cooling and potentially confound the interpretation of the results (Vissing *et al.* 1994). Skin-surface cooling can cause abrupt and dramatic decreases in SSNA, skin blood flow and sweat rate in heated individuals even before marked changes in internal or mean skin temperatures are identified (see Fig. 3). Third, the present study assessed sweat rate from non-glabrous skin on the dorsal aspect of the foot, which might exhibit different control of sweat rate relative to the chest and forearm which were assessed in the cited studies.

Pharmacological modulation of MAP did not change SSNA in either thermal condition. This finding is in agreement with some, but not all, previous research. In normothermic individuals direct stimulation of the carotid sinus nerve (Wallin *et al.* 1975), Valsalva manoeuvres (Delius *et al.* 1972b), LBNP (Vissing *et al.* 1994), or spontaneous variations in blood pressure (Hagbarth *et al.* 1972) fail to alter SSNA. However, less clear are conclusions regarding the effects of blood pressure modulation of SSNA in individuals with elevated SSNA due to heat stress. To investigate this question Macefield & Wallin (1996) measured single sudomotor axon discharge in moderately heated individuals during spontaneous fluctuations in blood pressure. They identified that some of these axons showed weak, but significant, correlation with spontaneous

fluctuations in cardiac interval and in diastolic blood pressure. These findings are similar in concept to findings by Dodt *et al.* (1995), which observed decreases in SSNA in mildly heated subjects during LBNP and during head-up tilt. In contrast, Vissing *et al.* (1994) did not see changes in SSNA during LBNP in mildly heated individuals when skin-surface cooling, which occurred during the application of LBNP, was controlled. Differences between these studies may be related to the method of heating, the magnitude of heating, the baroreceptor populations perturbed and/or the technique used to perturb the baroreceptors. The advantage of the present study is that relatively large decreases in MAP were accomplished in passively heated individuals without the potentially confounding influences of skin-surface cooling.

Another important difference between the present study and prior studies may be the relative difference in the unloading of specific baroreceptor populations. Both LBNP and upright tilt are likely to cause relatively greater unloading of the cardiopulmonary baroreceptors when compared to unloading of the arterial baroreceptors (i.e. carotid and aortic baroreceptors). In contrast, it is likely that with the present technique the arterial baroreceptors were unloaded to a greater relative extent than the cardiopulmonary baroreceptors given findings by Dibner-Dunlap *et al.* (1996) that central venous pressure does not change during bolus infusions of sodium nitroprusside and phenylephrine in healthy subjects. Previously, we and others were unable to demonstrate that carotid baroreceptor perturbations caused changes in cutaneous vascular conductance (Crandall *et al.* 1996) or SSNA (Wallin *et al.* 1975). Given these findings, a reasonable hypothesis would be that the lack of change in SSNA and sweat rate observed in the present study was due to the perturbation primarily unloading baroreceptor populations (i.e. carotid and aortic) that may not have an efferent limb governing SSNA or sweat rate. In contrast, changes in SSNA during head-up tilt or LBNP observed by others may be due solely to cardiopulmonary baroreceptor unloading (Dodt *et al.* 1995, Mack *et al.* 1995). Thus, differing responses between the present study and those previously reported may be due to the method of baroreceptor unloading.

The present study suggests that rapid and steady-state changes in arterial blood pressure do not modulate integrated multiunit SSNA. However, this finding is in contrast to prior work by Macefield & Wallin (1996) in which some single unit recordings of sudomotor SSNA showed a weak correlation with diastolic pressure and cardiac interval in heated individuals. These authors suggested that single unit recordings of sudomotor SSNA may be influenced by arterial baroreceptors. Differences in conclusions between the cited study and the present study are not clear, but may be related to differences in

firing/recording of single unit neurons during baroreceptor loading/unloading as opposed to recording integrated responses from multiunit SSNA.

### Limitations to the interpretation of the results

Upon completion of the bolus infusion protocol we could not exclude the possibility that the absence of a change in sweat rate in response to brief periods of baroreceptor unloading (i.e. bolus infusion) was due to the time period in which MAP was reduced relative to the potentially longer time course that may be necessary to observe a change in sweat rate following a change in blood pressure. However, the validity of this argument may be questioned given the lack of change in SSNA during these changes in blood pressure, which would not be expected to exhibit a similar delay if SSNA was modulated by baroreceptors. Nevertheless, to address this issue, in a separate protocol blood pressure was progressively reduced over a period of 8–10 min via steady-state infusions of sodium nitroprusside. Despite appropriate and sustained decreases in blood pressure, coupled with baroreflex-mediated increases in heart rate (see Table 3), no change in SSNA or sweat rate was observed in any subject regardless of the thermal conditions. Thus, it is unlikely that a lack of arterial baroreflex modulation of SSNA or sweat rate was due to the brief period in which arterial blood pressure was altered during the bolus infusion protocol.

Another potential limitation of the present study could be related to the magnitude of change in arterial blood pressure during bolus and steady-state infusions. With the present data we cannot exclude the possibility that the degree of arterial blood pressure modulation might have been insufficient to evoke a response in SSNA and/or sweat rate. However, this possibility is unlikely given the relatively large change in heart rate observed during drug administration (see Fig. 2 and Tables 2 and 3), which clearly indicates the baroreflexes were unloaded/loaded (Mancia & Mark, 1983).

In conclusion, pharmacological modulation of arterial blood pressure with sodium nitroprusside and phenylephrine did not change SSNA in either normothermia or during whole-body heating. Sweat rate was similarly unaffected by changes in arterial blood pressure during the heat stress. The lack of decrease in SSNA and sweat rate during pharmacologically induced changes in blood pressure suggests that arterial baroreceptors (i.e. carotid and aortic baroreceptors) are not involved in the regulation of these variables, thereby leaving the possibility that cardiopulmonary baroreceptors are responsible for modulating these responses. Conversely, an alternative hypothesis may be that baroreceptors in general are incapable of altering SSNA and sweat rate regardless of the thermal condition.

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