Evidence of differential control of renal and lumbar sympathetic nerve activity in conscious rabbits.

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Abstract:
We have explored the possibility that renal sympathetic nerve activity and vasomotor sympathetic nerve activity are differentially regulated. We measured sympathetic nerve activity (SNA) to the kidney and the hind limb vasculature in 7 conscious rabbits 6-8 days after the implantation of recording electrodes. Acute infusion of L-NAME (6mg/kg/min for 5 min) led to an increase in blood pressure (from 66 ± 1 mmHg to 82 ± 3 mmHg) and a decrease in heart rate (from 214 ± 15 bpm to 160 ± 13 bpm). L-NAME administration caused a significantly greater decrease in renal SNA than lumbar SNA (to 68 ± 14 % vs. 84 ± 4 % of control values respectively). Volume expansion (1.5ml/kg/min) resulted in a significant decrease in renal SNA to 66 ± 7% of control levels but no change in lumbar SNA (127 ± 20%). There was no difference in the gain of the baroreflex curves between the lumbar and renal SNA (maximum gain of -7.6 ± 0.4 n.u/mmHg for lumbar SNA vs. -7.9 ± 0.75 n.u/mmHg for renal SNA). A hypoxic stimulus (10% O₂ and 3% CO₂) led to identical increases in both renal and lumbar SNA (195 ± 40 % and 158 ± 21 % of control values respectively). Our results indicate tailored differential control of renal and lumbar SNA in response to acute stimuli.
Introduction:

Early concepts of autonomic control suggested a global uniform activation of sympathetic nerve activity (SNA) to all organs in response to a ‘fight or flight’ stimulus (3). The general convention was to refer to SNA as if the same signal travels to all organs but this has been replaced with a more organized model that emphasises differential control of sympathetic outflow to functionally specific targets (4, 22). Sympathetic nerve activity appears to be elevated in hypertension (9, 10) and half of the increase can be accounted for by increased noradrenaline spillover solely from the heart and the kidney (7, 8). The selective increase in cardiac and renal SNA indicates the importance of studying the differential control of nerve activity to better understand the control of blood pressure. The majority of evidence supporting differential control of sympathetic nerve activity has come from anaesthesitized experiments where sympathetic outflow to different organs in response to stimuli such as volume expansion and baroreceptor stimulation were measured.

Studies in anaesthesitized rabbits have shown that volume expansion leads to an inhibition of renal SNA (32). This reduction in renal SNA with volume expansion appears to be differentially regulated compared to SNA to other non-renal organs. Although volume expansion is also accompanied by a decrease in lumbar SNA, this decrease appears to be differentially regulated compared to the renal SNA response (33) although it must be mentioned that the two nerve activities were recorded in two separate sets of animals. It is pertinent to note that both these studies were conducted in anaesthesitized rabbits. Recent studies have indicated that anaesthesia can influence mean levels of sympathetic nerve activity (31), dampen reflex responses (23) and alter the cardiovascular responses to various stimuli. If the resting levels of nerve activity in the above studies were influenced by anaesthesia, it is possible that the differential responses observed may be a factor of the anaesthesia as opposed to a real differential response in SNA. It is important that the differential responses in nerve activity to volume expansion are reassessed in a conscious animal setting where the animals have recovered from the surgery and effects of stress are minimal.

In addition to volume expansion, researchers have also explored the differential control of SNA to baroreflex and chemo reflex stimulation. As indicated earlier, the level of anaesthesia and stress state of the animal can influence the mean levels of nerve activity and hence it is important that experiments involving SNA recordings to two organs are conducted in the same animal. An inability to directly record SNA to different organs for a long period of time has meant that the majority of studies have been conducted in anesthetized animals. These studies examining differential control of nerve activity
have been conducted in anaesthetized rat preparations and support differential control of nerve activities in response to baroreceptor stimulation (5, 29, 35). The mean level of nerve activity recorded varies depending on the nature of the contact between the nerves and the electrode. This has necessitated nerve activity levels being regularly expressed as a percentage of the control resting levels. Given that anaesthesia can influence the mean resting levels of nerve activity and dampen reflex responses (23), it is likely that the differential responses observed in response to baroreceptor stimulation are confounded by the anaesthetized state of the animals. It is important that a conscious animal preparation be used to examine the differential control of SNA and we have explored the possibility that renal sympathetic nerve activity and vasomotor sympathetic nerve activity are differentially regulated.

In order to better understand differential control of nerve activity, it is also important that different stimuli be used as some nerves can have a differential response to one set of stimuli but the same nerves could have similar responses to other stimuli. While volume expansion is associated with a decrease in renal SNA, chemoreceptor stimulation is associated with an increase in renal nerve activity in the anaesthetized rabbit preparation (13). We are not aware of any studies that have examined the response in lumbar SNA to hypoxia to indicate if the response in renal SNA is differentially modulated. Another aim of our experiments was to examine the differential control of SNA to chemoreceptor stimulation in a conscious animal preparation.

Recent evidence has indicated an important interaction between SNA and nitric oxide in modulating the mean levels of arterial pressure (30). It is unclear if nitric oxide differentially modulates SNA to different organs. The only previous study exploring this question was conducted in an anaesthetized rat preparation. Hirai et al. (12) observed similar reductions in both renal and lumbar SNA with inhibition of nitric oxide in baroreceptor intact animals. These responses in nerve activity have not been confirmed in a conscious animal preparation. As we have suggested previously, the presence of anaesthesia can affect mean levels of SNA and it is important to verify the differential responses in a conscious animal setting. In order to explore the possibility that renal SNA is selectively regulated, we have measured renal and lumbar sympathetic nerve activity responses to different acute stimuli in a conscious animal setting. We hypothesized that different acute stimuli would be accompanied by tailored differential responses in renal sympathetic nerve activity and vasomotor sympathetic nerve activity.
Methods:

Animal preparation. Experiments were conducted in New Zealand White rabbits with initial weights of 2.2–3.5 kg and were approved by the University of Auckland Animal Ethics Committee. The rabbits were housed individually in cages (height 45 cm, width 72 cm, and depth 72 cm). The rabbits were fed daily (100 g standard rabbit pellets, supplemented with hay, carrot, and apple) at 0900, and water was available ad libitum. The room was kept at a constant temperature (18°C) and dark-light cycle (lights on from 0600 to 1800).

Anesthesia was induced using intravenous administration of propofol (Diprivan, 10 mg/kg) followed by intubation and then maintenance with halothane. Nerve recording electrodes were implanted to record renal and lumbar sympathetic nerve activity. Implantation of electrodes to both regions was conducted in the same surgery. Procedures to implant the renal nerve electrodes have been described in detail previously (18). Briefly, a retroperitoneal incision was used to expose the left kidney and the renal nerve was identified and placed within a pair of coiled electrodes. The electrode wires and nerve were then coated in a silicone elastomer (Kwik-sil, World Precision Instruments, Florida, USA). The lumbar nerves were also approached via a left flank incision and a retroperitoneal approach. The lumbar nerves in the vicinity of the 3rd to 5th lumbar vertebrae were identified and placed within a pair of coiled electrodes. As with the renal nerve, the electrode and nerves were coated in a silicone elastomer. The free ends of the electrode wires were tunneled to the back of the neck and buried subcutaneously. All incisions were closed and the animal was then allowed to recover. After surgery the rabbits were treated prophylactically with an antibiotic (enrofloxacin, Baytril, Bayer, New Zealand;
5 mg/kg sc daily for 5 days) and analgesic (ketoprofen, Ketofen, Rhone Merieux, Essex, UK; 2 mg/kg sc daily for 3 days). As soon as the rabbits regained consciousness they were returned to their home cages. A heating pad was placed in the cage for 24 h after the surgery.

At least 6 days were allowed for the animals to recover from the surgery and resume normal eating and drinking habits. When normal eating and drinking patterns were established and the weights of the animals had returned to that previous to surgery, the acute experiments were performed. On the day of the experiment the rabbit was placed in a small box and catheters were inserted under local anesthesia into a central ear artery and connected to a pressure transducer for continuous arterial pressure measurements, and into the marginal ear veins for administration of drugs. The renal and lumbar nerve electrode wires were exteriorized and connected to the recording equipment. Renal and lumbar SNA was amplified, filtered between 50-5000 Hz, full-wave rectified and integrated using a low pass filter with a time constant of 20 ms. Once preparation was complete rabbits were left for at least 30 min before starting the experiment. The animals were subjected to acute interventions over two separate days at least 48 hours apart. On the first day, baroreflex responses and an acute infusion of L-NAME were carried out. On the second day, the animals were subjected to hypoxia and volume expansion. Appropriate time control experiments were conducted to ensure the SNA data collected was stable.

**Experimental protocol for day one.**

**Baroreflex responses.** After collecting a 5 min period of baseline recording, baroreflex responses were determined in response to infusions of phenylephrine and sodium nitroprusside. Sodium nitroprusside (1 mg.ml⁻¹) was slowly infused to reduce arterial pressure down to about 45 mmHg at a rate of 0.5-1mmHg/sec, all variables were then allowed to return to baseline before phenylephrine (1 mg.ml⁻¹) was infused to raise arterial pressure at a rate of 0.5-1mmHg/sec to between 120mmHg and 140mmHg (when sympathetic nerve activity was silent). These sequences were repeated at least 3 times.

**Acute blockade of nitric oxide.** Once recorded variables had returned to resting levels, a 5 min period of control data was collected before acute administration of L-NAME was carried out. L-NAME was infused at a dose of 6 mg/kg/min (in 3 ml saline) for 5 minutes through a marginal ear vein. Once the L-NAME was administered, a further 15 minutes of data was collected. The rabbit was then returned to its home-cage.

**Experimental protocol for day two.**
On a separate day at least 48 hours after the above protocols, the animals were prepared as above and exposed to hypoxia and volume expansion.

**Hypoxia.** The rabbit was placed within a box in a sealable Perspex chamber (volume 30L). The animals were allowed to rest inside the Perspex chamber which was initially open to room air for 10 min while control baseline data was collected. Once baseline data was collected, the chamber was closed to room air and then perfused through a small hole with a gas mixture of 10% O₂ and 3% CO₂ (makes a normocapnic hypoxic mixture) delivered at 10 L/min for 15 min. This was followed by a further 5 min of recovery data when the chamber was exposed to room air. Arterial blood samples (0.3 ml) were taken before and at the end of the hypoxic period.

**Volume expansion.** Once the response to hypoxia was recorded and variables had returned to baseline resting levels, a further 15 min was allowed before commencing the volume expansion protocol. A polygeline/electrolyte solution (Gelofusine (composition; succinylated gelatin, sodium chloride and sodium hydroxide: osmolality 283 mOsm/kg), Health Support Ltd., Auckland, New Zealand) was used to increase plasma volume. This was administered at room temperature at a rate of 1.5 ml/min/kg for 15 min (total volume infused was 55 ± 3 ml). Data continued to be collected for 15 min after the infusion was stopped.

**Data Collection:**
All data was sampled at 500 Hz using an analog-to-digital data acquisition card (AT-MIO64E-3 National Instruments, Austin, TX). All subsequent data analysis was performed using a data acquisition program (Universal acquisition and analysis ver 11; Telemetry Research, Uniservices Limited, Auckland, New Zealand). The 2s averages of MAP, lumbar SNA and renal SNA during the baroreflex curves were collected and a general non-linear regression program was used (26) to fit the collected MAP-lumbar SNA and MAP-renal SNA data to a sigmoidal logistic function to produce baroreflex curves. The program uses a 5 parameter non-linear regression equation to produce the resultant baroreflex curves. For the baroreflex curves, the sympathetic nerve values were normalised with the upper plateau with sodium nitroprusside being 100%. The noise levels were taken to be the integrated value when blood pressure was high with phenylephrine and no bursts were evident in the raw SNA signal.
Statistical Analysis. Apart from the baroreflex curves, all renal SNA and lumbar SNA values were normalized as a percent of the resting nerve activity recorded during the control period of each protocol. All data was analyzed using analysis of variance. The sum of squares was completely partitioned to account for all the variability in the data. Data are shown as the mean ± SEM. P values < 0.05 were considered significant.

Results:

Original neurograms from renal and lumbar SNA obtained under control conditions revealed a high degree of similarity between the bursting properties of each nerve activity (Figure 1). Direct voltages cannot be compared between nerves due to the variable nature of the contact between the nerve and recording electrode and the lumbar nerve being, in general, slightly smaller than the renal. However it was apparent that the individual frequency of bursts was very similar within each animal under control conditions.

Responses to blockade of endogenous nitric oxide

Both renal and lumbar SNA displayed a significant decrease following L-NAME administration. However the decrease in renal SNA was significantly greater than the decrease in lumbar SNA; reaching 68 ± 14 % of control values 10 minutes after the infusion ended vs. 84 ± 4 % for lumbar SNA (p<0.05). L-NAME administration led to a gradual increase in mean arterial pressure from 66 ± 1 mmHg during control levels to 82 ± 3 mmHg 10 minutes after the end of the infusion (p<0.05; Figure 2). This was accompanied by a decrease in heart rate from 214 ± 15 bpm to 160 ± 13 bpm 10 minutes after the end of the infusion.

Steady state changes during volume expansion.

Volume expansion resulted in a significant decrease in renal SNA (p<0.05) but no change in lumbar SNA (Figure 3). In the 5 min period following the infusion renal SNA was 78 ± 10 % of control levels whereas lumbar SNA was 110 ± 22 % of control levels. Renal SNA decreased further to 66 ± 7%
(maximum decrease of 43% and minimum decrease of 95% of control values) whereas lumbar SNA was 127 ± 20% of control levels (there was a decrease in one animal to 87% of control) in the 10-15 min period after infusion was stopped (p<0.05 vs. each other). Arterial pressure was unchanged (66 ± 1 mmHg) but heart rate was significantly increased by 18 ± 5 bpm (p<0.05).

*Baroreflex determination*

Baroreflex determination using rapid infusions of sodium nitroprusside and phenylepinephrine revealed that responses in the average levels of renal and lumbar SNA were the same. When the levels of SNA were reflected as a percentage of the maximum SNA obtained during sodium nitroprusside infusion it was apparent that the mean baroreflex curve was not significantly different between the nerves (figure 4 and Table 1) with a maximum gain of -7.6 ± 0.4 n.u/mmHg for lumbar SNA vs. -7.9 ± 0.75 n.u/mmHg for renal SNA.

*Hypoxia*

Hypoxia (10% O₂ and 3% CO₂) caused PaO₂ to fall from 100 ± 2 mmHg to 50 ± 5 mmHg. Significant increases in both lumbar and renal SNA was evident in all the animals (Figure 5). However, the renal and lumbar SNA responses were not different from each other. Renal SNA averaged 195 ± 40 % (maximum of 290% and minimum of 110%) and lumbar SNA averaged 158 ± 21 % of control values (maximum of 210 % and minimum of 120%) during the last 5 min of the 15 min hypoxia period. Both nerve activities returned back to normal when hypoxia was ceased. Hypoxia had no significant effect on either mean arterial pressure (66 ± 2 mmHg during control) or heart rate (204 ± 17 mmHg during control).

**Discussion:**
We have investigated the reflex control of both renal and lumbar SNA and have shown that renal and lumbar SNA are differentially regulated in response to certain stimuli (volume expansion and blockade of endogenous nitric oxide). However there is no difference in the response of renal and lumbar SNA to baroreceptor and chemoreceptor stimulation suggesting differential control of nerve activity does not occur in response to all stimuli. Our simultaneous recordings of renal and lumbar SNA in conscious rabbits extend observations from previous studies conducted in anaesthetized animals.

**Differential responses to increased blood volume**

Our results showing that renal SNA is particularly sensitive to volume expansion is consistent with the conclusions drawn from previous studies conducted in anaesthetized conditions. Studies in anaesthetised rabbits have shown that volume expansion is accompanied with a decrease in renal SNA (32). Studies in conscious rabbits have confirmed the decrease in renal SNA with volume expansion (2). The reduction in renal SNA seen in our study is similar to the one seen by Badoer et al. (50%) in their conscious rabbits (2). Whether volume expansion also results in a decrease in lumbar SNA in conscious animals was not determined previous to this study. We have simultaneously shown that while renal SNA decreased, lumbar SNA was unchanged with volume expansion. This is in contrast to a previous study in anaesthetized rabbits where the authors observed a decrease in lumbar SNA with volume expansion (33). The rate of volume expansion and the final volume administered in this study was comparable to our study. Volume expansion in both the previous anaesthetized preparation studies (32,33) was accompanied by an increase in mean arterial pressure in contrast to our study that showed no change in arterial pressure. The increase in mean arterial pressure would lead to a baroreflex mediated decrease in nerve activity in these studies which might help explain the decrease in lumbar SNA with volume expansion. Indeed sino-aortic denervation in these groups of animals greatly attenuated the lumbar SNA response but did not affect the renal SNA response suggesting the decrease in lumbar SNA was primarily baroreflex mediated (32,33). This might help explain the differences in lumbar SNA responses between our study and the previous study conducted in anaesthetized conditions. It is also unclear if the anaesthetized condition of the rabbit played a role in the different lumbar SNA responses observed. The reduction in renal SNA with volume expansion appears to be mediated by cardiopulmonary afferents as section of the cardiopulmonary afferents in anesthetized rabbits abolished the response (32). Administration of intrapericardial procaine to block cardiac afferents in conscious rabbits also blocks the sympathoinhibition in renal SNA to volume expansion (2). Our results suggest control of lumbar SNA is not governed to any large extent by cardiopulmonary afferent activity which supports findings from previous studies conducted in the anaesthetized rabbit.
Our results indicate volume expansion is accompanied by a tailored differential decrease in renal SNA compared with no change in lumbar SNA.

This differential inhibition of renal SNA compared to lumbar SNA does not appear to be confined to the rabbit. Weaver (36) showed in an anesthetized cat preparation that intravascular volume expansion inhibited renal SNA but has no effect on lumbar SNA. The inhibition in renal SNA was confirmed in a conscious cat preparation by Schad and Seller (28). Karim et al. (17) showed in an anaesthetized dog preparation that left atrial distension is accompanied with a decrease in renal SNA but no change in lumbar SNA. This differential SNA response in dogs has not been confirmed in a conscious preparation yet. It appears that in the rabbit, the cat and the dog, volume expansion is accompanied by a decrease in renal SNA but no change in lumbar SNA.

**Differential response to blockade of endogenous nitric oxide**

Administration of L-NAME was accompanied by a significant decrease in both renal and lumbar SNA (68% and 84% of control respectively). The only previous study that examined the differential response in renal and lumbar SNA to NO inhibition was conducted in an anesthetized rat preparation. Hirai et al. (12) examined the differential responses of lumbar and renal SNA to nitric oxide inhibition and observed a reduction in both renal (-45% of control) and lumbar SNA (-35% of control) with L-NAME administration. In contrast to our findings, they did not observe any significant differences between the responses in renal vs. lumbar SNA. It is unclear if the differences between the studies are due to the different species involved or the anaesthetized condition of the rat preparation. The L-NAME administration in the rat study was also less (20mg/kg) compared to our study (30mg/kg) which may be another reason for the differences observed. We acknowledge that comparison between studies where L-NAME administration is used is further made difficult because of the complex central as well as peripheral effects of NO on SNA (11, 34, 38).

One of the novel aspects of our study is that we have determined the baroreflex and NO effects on renal and lumbar SNA in the same animal. We believe much of the decrease in SNA with L-NAME administration can be attributed to the arterial baroreflex. L-NAME caused blood pressure to increase by 16 mmHg; using data collected from baroreflex determination (Figure 4) indicates that such an increase in blood pressure would be expected to decrease nerve activity to 70% of control nerve activity. Given the actual change in renal SNA was to 68% of control, we suggest that the decrease in
renal SNA is most likely baroreflex mediated. In support of a baroreflex mediated decrease in renal SNA, Liu et al. (19) showed that the decrease in renal SNA in response to nitric oxide blockade could be reversed by abolishing the change in blood pressure in the conscious rabbit. The decline in lumbar SNA (84% of control) was less than expected if the arterial baroreflex was the only contributing factor. As renal and lumbar SNA had identical baroreflex responses (Figure 4) we suggest that NO differentially modulates the lumbar and renal SNA response. Our results support the possibility that nitric oxide differentially modulates sympathetic nerve activity to the kidney and the hind limb vasculature. It is difficult to extend our results indicating differential modulation of SNA by NO to chronic conditions due to lack of a chronic stimulus in our studies. Clearly, further studies are needed to explore the possibility of differential control of renal SNA with long-term changes in blood volume and nitric oxide levels.

**Baroreflex and chemoreflex control of SNA**

The use of a conscious animal setting in our study where nerve activity to both the kidney and the hind limb region are measured at least 6 days after surgery is a major improvement on previous studies as SNA responses can be affected by anaesthesia (6, 31). Indeed differences in the gain of the renal SNA response to baroreceptor stimulation has been observed between conscious and anaesthetized rabbits (15). Our findings show that baroreflex control of renal and lumbar SNA are identical (Figure 4 and table 1). It is problematic to compare nerve activities between animals and this necessitates recordings of SNA from different organs in the same animal. Very few studies have examined the differential control of SNA by recording more than two nerve activities in the same animal and these studies have primarily been conducted in anaesthetized rats. In contrast to our study, Scislo et al. (29) observed a steeper gain for the renal SNA baroreflex curve compared to the lumbar SNA baroreflex curve in the anesthetized rat. The conscious state of the animal in our study is an improvement on this previous study as the anesthetized condition of the rat might lead to a depressed baroreflex response and may account for the differences observed. Apart from the steeper gain for the renal SNA baroreflex, the authors conclude that there is no difference between the functions of renal and lumbar SNA in the range of mean arterial pressure close to the operating point which is in agreement with our findings. We cannot discount the possibility that in the rat, the gain of the renal SNA baroreflex curve is steeper compared to the lumbar SNA baroreflex curve. To date, differential control of lumbar vs. renal SNA has not been examined in the conscious rat and it is unclear if the species difference or the difference in the anaesthetized state of the animal accounts for the different gains observed. The only other study in anaesthetized rats compared renal vs. adrenal SNA in the anaesthetized rat and found similar gain
values (35). The different nerves being compared makes it difficult to make meaningful comparisons between the studies.

One previous study has examined differential control of SNA in a conscious animal preparation (24, 25). These authors examined the baroreflex control of sympathetic nerve activity to the heart and the kidney in a conscious cat preparation and reported a significant difference in the gain of cardiac and renal SNA baroreflex responses. It is difficult to compare the results of this study with our study as different nerves were being compared and the species being studied is also different. In addition, the experimental approach used to calculate gain in these studies was different to our study. The baroreflex gain in these conscious animals was calculated with injection of norepinephrine and recording the resultant changes in blood pressure and nerve activity. As such, the gain obtained would represent the portion of the baroreflex curve above the resting point. Our study included both an increase and a decrease in blood pressure and we believe this gives a truer representation of baroreflex gain.

Exposure of the animals to hypoxia led to a similar increase in both renal and lumbar SNA suggesting no difference between the two nerves in the response to chemoreceptor activation. Our results confirm previous studies in anaesthetized (13) and conscious (20, 21) rabbits that have indicated an increase in renal SNA with chemoreceptor stimulation. We are not aware of any studies that have examined responses in lumbar SNA to chemoreceptor stimulation previous to this study. Interestingly, arterial hypoxia leads to inhibition of cardiac sympathetic nerve activity in the anaesthetized rabbit (13, 14) and the rat as evidenced by a decrease in cardiac norepinephrine turnover (16). Thus while our results showed no differential response in the renal and lumbar SNA response, it does appear that moderate chemoreceptor stimulation leads to differential inhibition of cardiac SNA.

We have observed differential regulation of renal and lumbar SNA in response to volume expansion and L-NAME administration. Recordings of lumbar SNA include a significant number of pre-ganglionic neurons whereas renal nerves consist of almost entirely postganglionic neurons. It is possible that the differential regulation seen is attributable to differences in modulation of ganglionic transmission and therefore recorded renal SNA and lumbar SNA. Volume expansion will lead to suppression of angiotensin II and angiotensin II can modulate ganglionic transmission (27). Nitric oxide levels have been shown to modulate ganglionic transmission as well although some controversy still exists (37). It is possible that changes in angiotensin II and NO levels may have influenced
ganglionic transmission and we cannot discount this possibility as the reason for the differential responses seen.

**Perspectives:**

Differential regulation of sympathetic nerve activity could play an important role in the long-term control of blood pressure. There is now strong evidence to indicate an increase in sympathetic nerve activity which may play a critical role in the development of hypertension (1, 9, 10). Interestingly, half of the increase in total noradrenaline spillover seen in essential hypertension can be accounted for by increased noradrenaline spillover from the heart and the kidney (7, 8). This highlights the differential control of nerve activity where increases in SNA to selected organs may be a critical factor in the development of hypertension. The finding that sympathetic nerve activity to different beds is differentially regulated in the short term raises the possibility whether renal SNA could be differentially controlled in the long term. It is equally possible that lumbar SNA might be differentially increased in the long term leading to increased peripheral resistance that may maintain the high blood pressure. Clearly further studies are needed to explore the importance of differential control of renal SNA in the long-term control of blood pressure.
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References:


Figure Legends:

Figure 1: Original and integrated lumbar and renal sympathetic nerve activity (SNA) during control conditions (top panel) and sodium nitroprusside administration (bottom panel) in one rabbit. The integrated SNA values are expressed in arbitrary units (a.u). (Int - Integrated)

Figure 2: Responses in arterial pressure, heart rate, renal sympathetic nerve activity (open circles) and lumbar sympathetic nerve activity (closed circles) to L-NAME administration at 6mg/kg/min. Dotted lines denote L-name administration. The SNA values are expressed as a percentage of the control period of 5 minutes. Data shown are mean ± SEM. * - denotes significant effect of L-NAME administration (p<0.05). # - denotes significant difference between the groups.

Figure 3: Responses in arterial pressure, heart rate, renal sympathetic nerve activity (open circles) and lumbar sympathetic nerve activity (closed circles) during volume expansion (1.5 ml/min/kg for 15 min) in a group of 7 rabbits. The SNA values are expressed as a percentage of the control period of 5 minutes. Volume expansion resulted in a significant decrease in renal SNA but no change in lumbar SNA. Data shown are mean ± SEM. * - denotes significantly different from control (p<0.05). # - denotes significant difference between the groups.

Figure 4: Mean baroreflex curves (n=7) relating the MAP-LSNA (solid line) and the MAP-RSNA (dotted line). Symbols represent the resting points of the curve with the respective SEMs. The sympathetic nerve values are expressed in normalised units (n.u) as a percentage of the upper plateau. The upper plateau in both curves is 100 n.u. Inset shows the gain of the baroreflex curves at different blood pressures. ● - represents resting point for the MAP-LSNA baroreflex curve and for the MAP-same).

Figure 5: Responses in arterial pressure, heart rate, renal sympathetic nerve activity (open circles) and lumbar sympathetic nerve activity (closed circles) to 15 minutes of hypoxia (10% O₂ and 3% CO₂)
showing an increase in both renal SNA and lumbar SNA. The SNA values are expressed as a percentage of the control period of 5 minutes. Data shown are mean ± SEM. * - denotes significant effect of hypoxia (p<0.05).
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<th>Lumbar SNA-BP baroreflex curve parameters</th>
<th>Renal SNA-BP baroreflex curve parameters</th>
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<td>Lower plateau (n.u)</td>
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<td>Range (n.u)</td>
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<td>Lower plateau curvature</td>
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<td>BP_{50} (mmHg)</td>
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<td>Upper plateau curvature</td>
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<td>Mean arterial pressure (mmHg)</td>
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<td>SNA (n.u)</td>
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Table 1: Table showing the baroreflex parameters of the MAP-lumbar SNA and MAP-renal SNA baroreflex curves. The baroreflex parameters are expressed in normalised units (n.u) as a percentage of the upper plateau. Data shown are mean ± SEM.