Journal of Thermal Biology 66 (2017) 10–16

Contents lists available at ScienceDirect

Journal of Thermal Biology

journal homepage: www.elsevier.com/locate/jtherbio

Sinoaortic denervation attenuates vasopressin-induced hypothermia and reduction of sympathetic nerve activity innervating brown adipose tissue in rats

Yong-Lu Yang[a,*], Xin Liu[b], Rong Luo[a], Jian-Hui Xu[a], Chang Liu[a]

[a] Thermoregulation and Inflammation Laboratory, Chengdu Medical College, Chengdu, Sichuan 610500, China
[b] Department of Intensive Care Unit, First Hospital of Lanzhou University, Lanzhou, Gansu 730030, China

ARTICLE INFO

Key words:
Arginine vasopressin
Hypothermia
BAT sympathetic nerve activity
BAT thermogenesis

ABSTRACT

It is well known that sympathetic nerve activity innervating brown adipose tissue (BAT sympathetic nerve activity) plays an important role in BAT thermogenesis. We have found that peripheral administration of arginine vasopressin (AVP) induced hypothermia by reduced thermogenesis in BAT. However, little is known about AVP-induced hypothermic response and its relationship with BAT sympathetic nerve activity. Because increases in baroreceptor inputs inhibit peripheral sympathetic nervous activity, we hypothesized that AVP-induced hypothermia is related to baroreceptor reflex suppression of BAT sympathetic nerve activity. To test this hypothesis, Male Sprague-Dawley rats were subjected to sinoaortic denervation or sham denervation, and implanted with radiotelemetry transmitters to assess the effects of peripheral administration of AVP on BAT sympathetic nerve activity, core and BAT temperatures. In sham-operated rats, an intraperitoneal (i.p.) injection of 10 μg/kg AVP led to a significant decrease in core and BAT temperatures. However, sinoaortic denervation significantly reduced the fall of core and BAT temperatures induced by AVP, compared with levels in sham-operated rats. AVP (10 μg/kg i.p.) rapidly decreased BAT sympathetic nerve activity in control and sham-operated rats, with the greatest levels of suppression occurring at 35 min and these lowest levels attained were with 30.6% and 29.24%, respectively. Furthermore, we found that sinoaortic denervation attenuated the suppressive effects of AVP (10 μg/kg i.p.) on BAT sympathetic nerve activity. The greatest level of suppression was only 20.8% occurring at 35 min after AVP. Therefore, these results indicate that the hypothermic effects of peripheral administration of AVP are partially mediated by the arterial baroreceptor reflex suppression of BAT sympathetic nerve activity and BAT thermogenesis.

1. Introduction

A number of studies have demonstrated that the arginine vasopressin (AVP) plays an important role in thermoregulation (Drago et al., 1997; Pittman et al., 1998; Steiner et al., 1998; Yang et al., 2013). Both the central (Drago et al., 1997; Pittman et al., 1998) and peripheral (Steiner et al., 1998; Yang et al., 2012, 2013) administration of AVP cause a reduction in core temperature of normothermic rats. We found that the plasma AVP level was also significantly elevated when core temperature decreases during the light phase, suggesting that endogenous AVP is involved in the circadian changes of core temperature in rats (Yang et al., 2012). Endogenous AVP, acting through V1a receptors, could also be involved in tonic thermoregulatory processes, because V1a receptor antagonist elevates core and brown adipose tissue (BAT) temperatures during the light period (Steiner et al., 1998; Yang et al., 2012, 2013).

Several studies have assessed the mechanism by which AVP evokes the hypothermia. Evidence suggests that the ionotropic receptors of L-glutamate in the central nervous system participate in peripheral AVP-induced hypothermia by affecting heat loss through the tail (Paro et al., 2003). It has been reported that sinoaortic baroreceptor reflexes are involved in the control of core and skin temperatures (Zhang et al., 2003), because peripheral administration of vasopressor substances such as norepinephrine and phenylephrine suppresses heat production through the sinoaortic baroreceptor reflex (Shibata, 1982; Shibata et al., 1982). In addition, sinoaortic denervation attenuated the suppressive effects of angiotensin II on BAT thermogenesis and core temperature, and prevented enhanced heat loss induced by central cholinergic stimulation (Shido et al., 1985; Pires et al., 2010).

BAT thermogenesis is a significant component of the homeostatic

* Corresponding author.
E-mail address: ylyang9@sohu.com (Y.-L. Yang).

http://dx.doi.org/10.1016/j.jtherbio.2017.03.008
Received 27 November 2016; Received in revised form 13 March 2017; Accepted 13 March 2017
Available online 19 March 2017
0306-4565/ © 2017 Published by Elsevier Ltd.

repertoire to maintain body temperature during the challenge of low environmental temperature in many species from mouse to human, and plays a key role in elevating body temperature during the febrile response to infection (Morrison and Madden, 2014). BAT's potential metabolic role has been recognized to the extent that it is considered as a potential site for drugs aimed at altering energy expenditure (Tseng et al., 2010; Mund and Frishman, 2013). Neural activity of sympathetic nerve innervating brown adipose tissue (BAT sympathetic nerve activity) plays an important role in thermogenesis (Morrison and Madden, 2014). However, little is known about AVP-induced hypothermic response and its relationship with BAT sympathetic nerve activity.

Considering the evidence that increases in baroreceptor inputs inhibit peripheral sympathetic nervous activity (Shibata, 1982) and peripheral administration of AVP induced hypothermia by reduced thermogenesis in BAT (Paro et al., 2003; Yang et al., 2012), we hypothesized that AVP-induced hypothermia is related to baroreceptor reflex suppression of BAT sympathetic nerve activity and BAT thermogenesis. Therefore, in the present study, we first assessed the effects of peripheral administration of AVP on core and BAT temperatures, and its relationship with BAT sympathetic nerve activity. Subsequently, we examined the effect of sinoaortic denervation on AVP-induced hypothermia and BAT sympathetic nerve activity in the rat.

2. Materials and methods

2.1. Animals and drugs

Adult male Sprague-Dawley rats weighing 230–320 g (Institute of Laboratory Animal Sciences, Sichuan Academy of Medical Sciences, China) were used for the experiments. The rats were housed individually in acrylic cages lined with wood shavings at an ambient temperature of 22 °C, relative humidity of 50%, and a standard 12:12-h light-dark cycle (lights on at 06:00 h). Animals were allowed free access to water and food. All animal studies were complied with the WHO Guidelines of Humane Use and Care of Animals and approved by Institutional Animal Use and Care Committee. AVP was purchased from Sigma Chemical Co. (St Louis, MO). AVP was dissolved in pyrogen-free sterile saline into a stock solution of 10 μg/ml and stored at –30 °C until the day of an experiment.

2.2. Experimental groups

Two sets of experiments were conducted to achieve the goals of present study. The first set was performed to investigate the effects of peripheral administration of AVP on core and BAT temperatures, and its relationship with BAT sympathetic nerve activity. The second set was performed to determine the influence of sinoaortic denervation on AVP-induced hypothermia and BAT sympathetic nerve activity in the rat.

2.3. Implantation of radiotelemetry transmitters

Core and BAT temperatures were simultaneously measured in undisturbed rats using dual probe transmitters (Data Sciences International, Model TL10M2-F40-TT). The animals were surgically implanted with radiotelemetry transmitters as described previously (Yang et al., 2012). Briefly, rats were anesthetized with an intraperitoneal injection of sodium pentobarbital (40 mg/kg). The transmitter body and dual probe transmitters were placed in the abdominal cavity. A small hole was made in the side of the abdominal wall and the tip of interscapular BAT temperature probe was passed through this incision. The tip of the temperature probe (148 mm wire lead with a 3 mm tip diameter) was threaded out subcutaneously to position under interscapular BAT. Following surgery, rats were administered a penicillin antibiotic (20,000 units; intramuscularly), and allowed at least 7 days of recovery before testing.

2.4. Sinoaortic denervation

After completion of transmitter implantation, sinoaortic denervation was performed according to the method described previously (Pires et al., 2010). Shortly after an intraperitoneal injection of atropine sulfate (3 mg/kg), a midline incision was made in the ventral region of the neck, and the superior laryngeal, aortic depressor, cervical sympathetic nerves, and the carotid sheath were sectioned. The fibers and connectives tissues of the wall of the carotid artery were stripped around the bifurcation area on both sides. These were then painted with a 10% phenol (in 95% ethanol) solution to remove any baroreceptor afferents that might remain. In controls rats, a sham-operation was performed by making a longitudinal incision at the cervical region. The nerves that had been sectioned in denervated group were exposed and put in place again, without being sectioned.

2.5. Measurement of core and BAT temperatures

In all experimental protocols, the environmental chamber was set at 22 °C. The rats were placed in clean cages with wood shavings at 17:00 h. The rats were allowed to adapt to the chamber overnight. The following day the rats were administered intraperitoneally with the AVP (10 μg/kg) or saline (1 ml/kg) at 10:00 h. Core and BAT temperatures were monitored in free-moving rats using radiotelemetry (Data Sciences International, St. Paul, MN, USA) for at least 4 h prior to dosing. A cross over design was utilized in this study and the rats were tested 10 days later. The rats that had been given saline were then dosed with AVP; the rats that had been given AVP were then given saline. The output of the transmitter was monitored at 5 min intervals by a receiver board placed under each rat's cage. Data were monitored on-line as well as stored on computer for later analysis.

2.6. Electrophysiological recordings of BAT sympathetic nerve activity

Rats were subjected to sinoaortic denervation or sham denervation. After 7 days, BAT sympathetic nerve activity was performed as described previously (Yasuda et al., 2005). Briefly, the rats were anesthetized intraperitoneally with urethane (0.85 g/kg) and α-chloralose (0.05 g/kg), a 2 cm dorsal interscapular incision made, BAT and connective tissue resected exposing nerves innervating BAT. The distal end of the nerve was ligated, and then microsurgical transection of small nerve fibre bundles hooked up with a pair of silver wire electrodes. At an ambient temperature of 22 °C, colonic temperature was monitored using a digital thermometer inserted 5 cm into the colon and was maintained at 37.0 ± 0.5 °C using JR-1/2-DC electrical heating pad (Chengdu Taimeng Sorftware Co. LTD). The spontaneous activity of BAT sympathetic efferent nerves were recorded by BL-420S Data Acquisition and Analysis System (Chengdu Taimeng Sorftware Co. LTD). The recording electrodes were immersed in a pool of liquid paraffin oil to prevent dehydration of the nerve tissue and for electrical insulation. After being placed on the recording electrodes, the rat was allowed to stabilize for 30 min. Throughout the course of the experiment, to provide a natural stimulus for the activation of the sympathetic nerve discharge to BAT, body temperature was lowered once in each animal by turning off the heat sources. This caused body temperature to fall from 37.0 °C to between 34 and 35 °C (Morrison et al., 2000; Madden and Morrison, 2010). Baseline measurements of spontaneous efferent nerve activity were made for 30 min just before intraperitoneal administration of AVP 10 μg/kg (10 μg/ml saline) or saline 1 ml/kg. After the injection, BAT sympathetic efferent nerve activity was recorded for 180 min.

2.7. Statistical analysis

Values of the BAT sympathetic nerve activity, core and BAT temperatures were expressed as the changes from basal values. Data

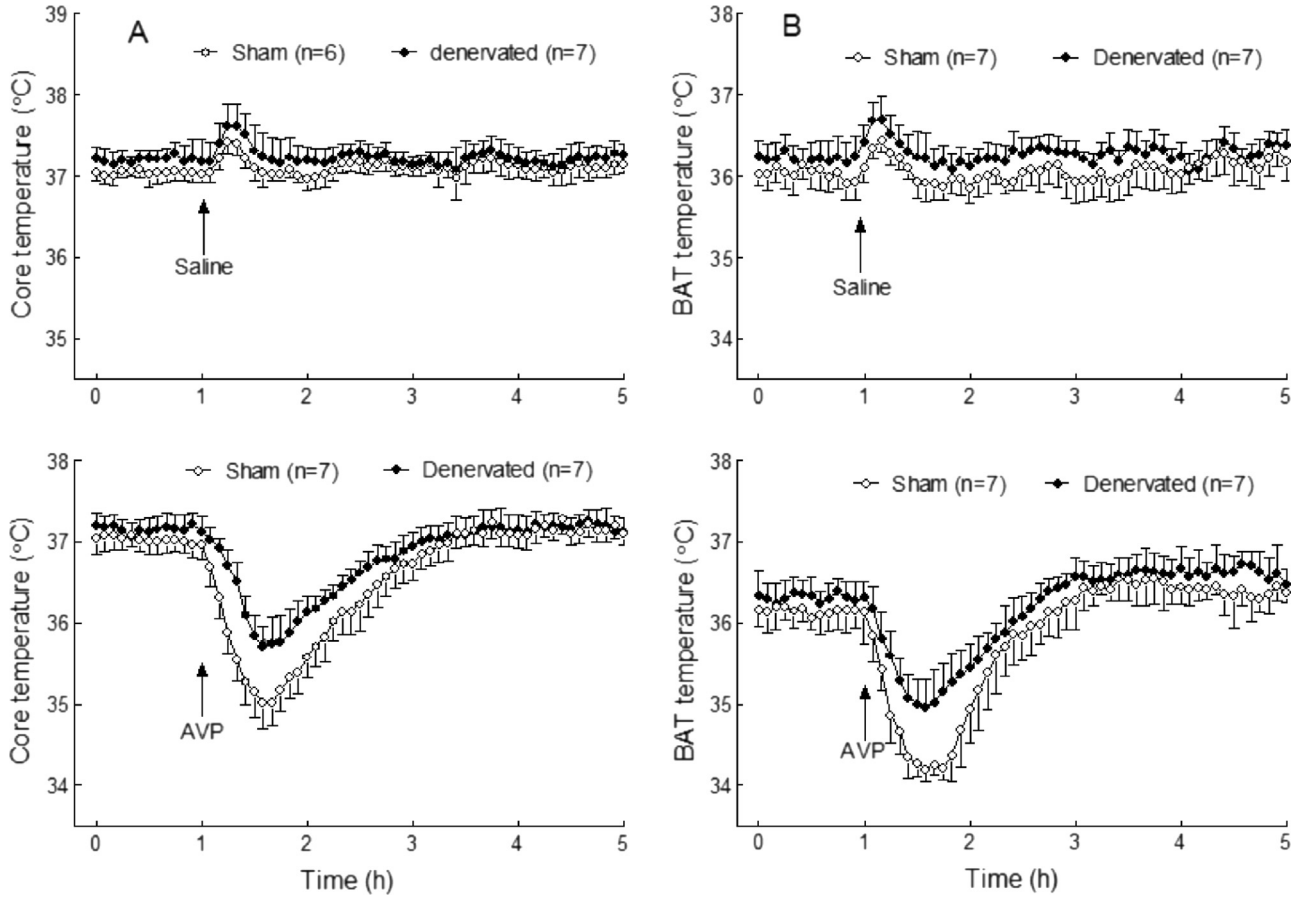

Fig. 1. Simultaneous telemetric monitoring of the time course for effect of AVP (10 μg/kg i.p.) on core (A) and BAT temperatures (B) in sham operated and denervated rats. Data were plotted as mean ± S.E. Denervated rats attenuated the hypothermic effects of intraperitoneal injection of AVP on core and BAT temperatures. ANOVA of sinoaortic denervation on temperature response to AVP for 90 min: core temperature: denervated rats *vs.* sham operated rats, $P < 0.01$; BAT temperature: denervated rats *vs.* sham operated rats, $P < 0.01$.

were plotted as mean ± S.E. These data were analyzed over the 90 min period starting from the time of injection of drugs. This time period represents the time of maximum change in BAT sympathetic nerve activity, core and BAT temperatures following drug administration. Data were analyzed statistically by ANOVA followed by multi-range test to assess differences between groups. Values of $P < 0.05$ were considered to be significantly different.

3. Results

3.1. Effect of sinoaortic denervation on hypothermic response induced by intraperitoneal injection of AVP

In all experimental protocols, core temperature ranged from 37.04 ± 0.21 °C (mean ± S.E.) to 37.28 ± 0.16 °C during the control period. No difference in initial core temperature values was observed among the different groups (Fig. 1). Administration of saline led to a transient elevation in core temperature that was attributed to the stress of handling and injection procedure (Fig. 1), because restrained rats reduce heat loss and increase heat production (Gordon et al., 2002; Dallmann et al., 2006). Approximately 50 min after dosing, core temperature returned to near baseline levels.

The effects of AVP on core temperature in the sham-operated and denervated rats are shown in Fig. 1A and Fig. 2A. In sham-operated rats, treatment with 10 μg/kg AVP caused a significant drop in core temperature, reaching a nadir of 35.01 ± 0.31 °C at 35 min after administration. In the denervated group, however, rats dosed with AVP also had a decrease in core temperature, reaching a nadir of 35.69 ± 0.25 °C at 35 min after administration, but the decrease was markedly less than that of sham-operated rats (1.46 ± 0.32 °C AVP-denervated rats vs. 2.04 ± 0.23 °C AVP- sham-operated rats, 35 min after injection; $P < 0.01$).

3.2. Effect of sinoaortic denervation on changes in BAT temperature induced by intraperitoneal injection of AVP

Fig. 1 shows that time course of BAT and core temperatures were simultaneously measured in rats using dual probe transmitter's temperature probe. BAT temperature ranged from 36.08 ± 0.11 °C to 36.31 ± 0.09 °C during the control period, the mean BAT temperature was 0.97 °C lower than core temperature (Figs. 1 and 3), and the decreases in BAT temperature preceded the decreases in core temperature (Fig. 3B). The duration of the hypothermic response in BAT temperature was shorter than corresponding core temperature, and the recovery from AVP-induced hypothermic responses in BAT was more rapid compared with core temperature (Fig. 3B). Administration of the saline led to a transient elevation in BAT temperature that was attributed to the stress of handling and injection procedure (Figs. 1B and 3A).

In sham-operated rats, administration with 10 μg/kg AVP led to a significant decrease in BAT temperature that persisted for over 90 min. The mean BAT temperature was 1.95 ± 0.30 °C lower than control levels at 35 min after administration (Figs. 1B and 2B). The amplitude of the hypothermic response in BAT temperature following AVP was similar to that of core temperature. However, in denervated rats, AVP injection induced less decreases in BAT temperature compared with the sham-operated rats (1.26 ± 0.29 °C AVP-denervated rats vs. 1.95 ± 0.30 °C AVP-sham-operated rats; $P < 0.01$; Figs. 1B and 2B) at

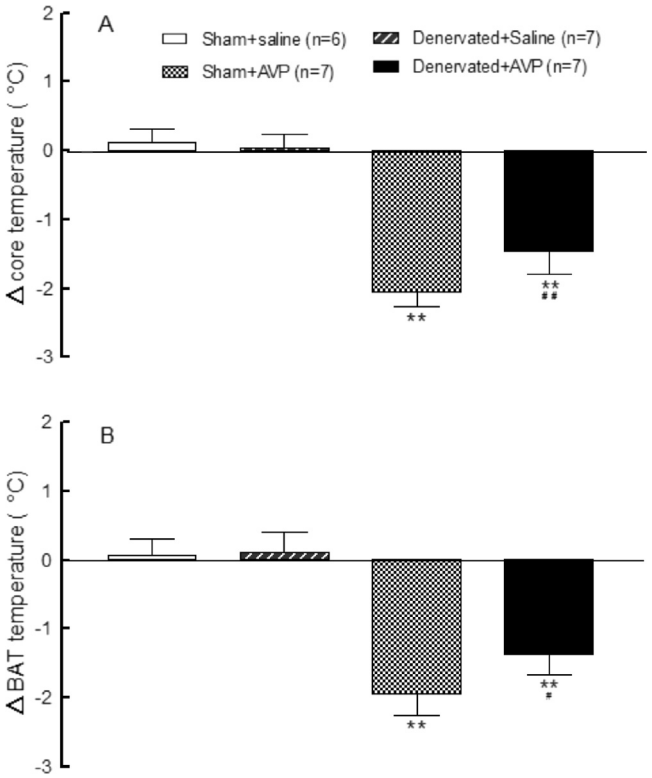

Fig. 2. Changes in core (A) and BAT temperatures (B) of sham operated and denervated rats following intraperitoneal injection of saline (1 ml/kg) or AVP (10 μg/kg). Temperature changes were calculated from data measured at 35 min after treatment (see Fig. 1). $^{*}P < 0.005$, $^{**}P < 0.001$ *vs.* sham operated + saline and denervated + saline group, respectively; $^{\#}P < 0.05$, $^{\#\#}P < 0.005$ *vs.* sham operated + AVP group.

the same time.

3.3. Effect of intraperitoneal injection of AVP on BAT sympathetic nerve activity

Fig. 4A shows the typical response of BAT sympathetic nerve activity after peripheral administration of AVP. The mean changes in BAT sympathetic nerve activity induced by AVP are shown in Fig. 4B. BAT sympathetic nerve activity rapidly decreased after peripheral injection of AVP, with the greatest level of suppression (30.6%) occurring at 35 min (Fig. 4B). Approximately 120 min after dosing, BAT sympathetic nerve activity recovered toward baseline levels. In contrast, injection of saline did not cause a significant alteration in the levels of BAT sympathetic nerve activity.

3.4. Effect of sinoaortic denervation on changes in BAT sympathetic nerve activity induced by intraperitoneal injection of AVP

Fig. 5 shows the typical response of BAT sympathetic nerve activity in sham-operated and denervated rat. The mean changes in BAT sympathetic nerve activity induced by AVP are shown in Fig. 6. In sham-operated rats, the level of BAT sympathetic nerve activity was significantly reduced by intraperitoneal injection of AVP, with the greatest level of suppression (29.24%) occurring at 35 min after AVP (Figs. 5A and 6B). Sympathetic nerve activity recovered toward baseline levels at 120 min after administration of AVP. The change in BAT sympathetic nerve activity following AVP was similar to that of rats without sham-operation (Fig. 4).

However, sinoaortic denervation attenuated the suppressive effects of intraperitoneal injection of AVP on BAT sympathetic nerve activity, the greatest level of suppression was only 20.8% occurring at 35 min after AVP (Figs. 5B and 6B). These changes differed significantly from

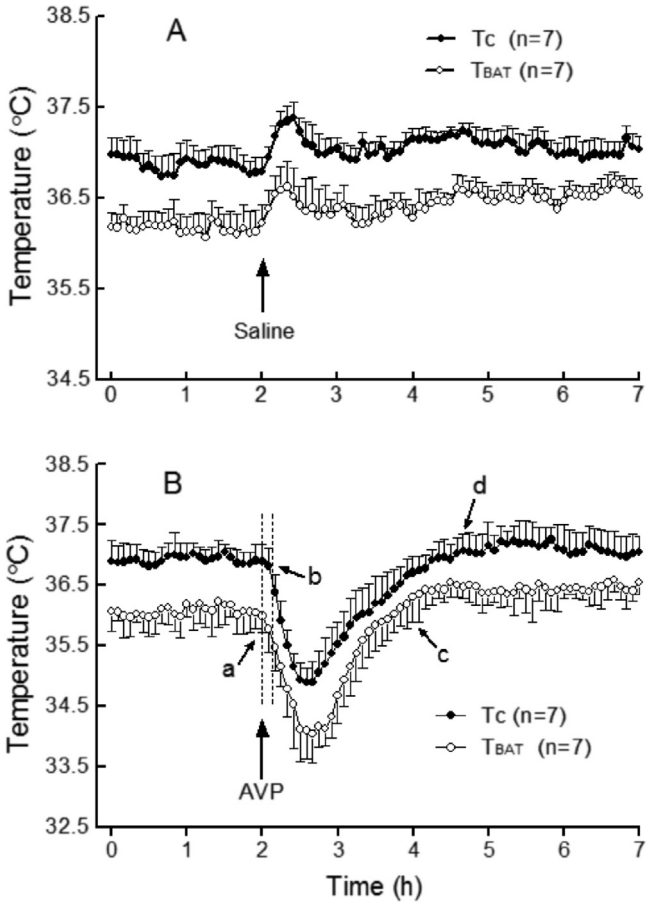

Fig. 3. Simultaneous telemetric monitoring of the time course for effect of AVP on core temperature (T_c) and BAT temperature (T_{BAT}) in rats. The decreases in T_{BAT} (a) preceded the decreases in T_c (b), and the recovery from hypothermic responses in T_{BAT} (c) was more rapid compared with T_c (d).

those induced by AVP in sham-operated rats ($P > 0.05$). Approximately 75 min after dosing, BAT sympathetic nerve activity recovered toward baseline levels. The duration of the suppressive effects in BAT sympathetic nerve activity was shorter than sham-operated rats (Figs. 5B and 6B; $P < 0.01$).

4. Discussion

The main finding of the present study was that the hypothermic effects of peripheral administration of AVP could be related to the carotid sinus baroreceptor reflex suppression of BAT sympathetic nerve activity and the decrease of BAT thermogenesis. This is supported by the following three new key findings: (1) the hypothermic effect of intraperitoneal injection of AVP is accompanied by a decrease in BAT temperature, (2) peripheral administration of AVP rapidly decreased BAT sympathetic nerve activity, and (3) sinoaortic denervation attenuated the suppressive effects of peripheral administration of AVP on BAT sympathetic nerve activity, core and BAT temperatures.

The changes in BAT temperature reflect changes in BAT metabolic thermogenesis, because the primary function of BAT is to produce heat to maintain body temperature constant (Richard and Picard, 2011; Yang et al., 2013; Morrison and Madden, 2014). However, previous studies were performed using the thermistor or single probe transmitter, core and BAT temperatures could not be simultaneously measured in the same animal (Shibata, 1982; Shido et al., 1984; Zhang et al., 2003). In the present experiments, core and BAT temperatures were simultaneously measured in rats using dual probe transmitters. The amplitude of the hypothermic response in BAT temperature following

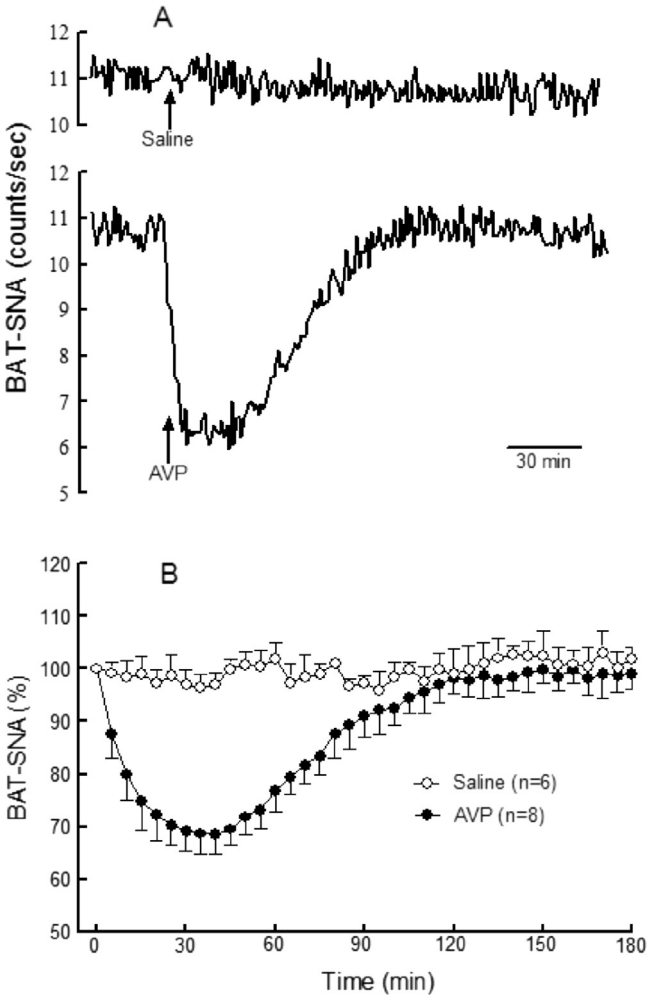

Fig. 4. Effects of intraperitoneal injection of AVP on BAT sympathetic nerve activity (BAT-SNA). A: representative trace data from recordings of BAT-SNA after administration of saline (1 ml/kg) or AVP (10 μg/kg). Arrowheads indicate the injection point; Horizontal bars, 30 min time scale. B: BAT-SNA after administration of AVP are expressed as mean ± S.E. of percentages of values at 0 min. ANOVA results of AVP (10 μg/kg) for 90 min: $P < 0.001$, significant difference compared to saline group.

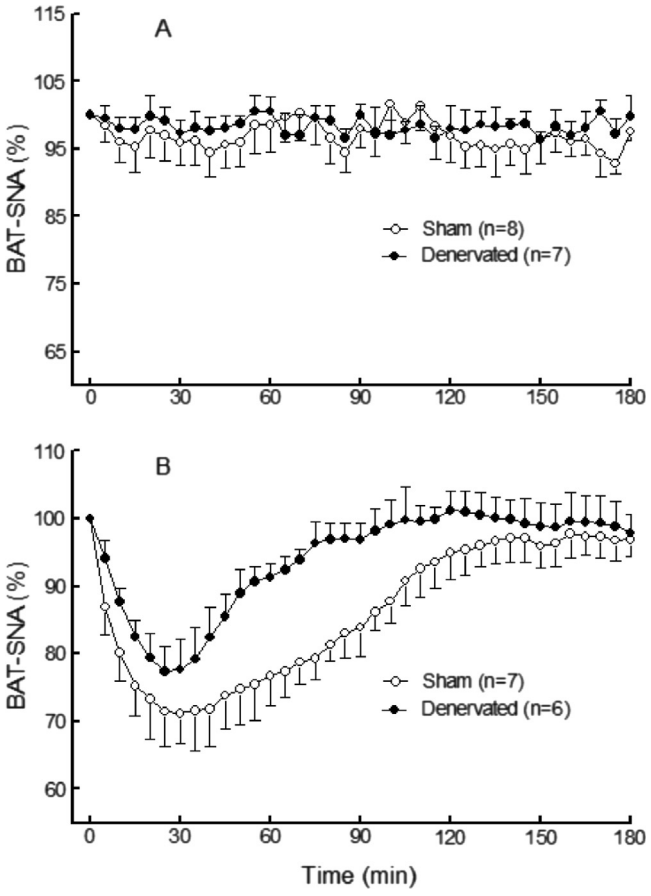

Fig. 6. Effect of sinoaortic denervation on changes in BAT sympathetic nerve activity (BAT-SNA) by intraperitoneal injection of saline (A) or AVP (B). BAT-SNA after administration of saline (1 ml/kg) or AVP (10 μg/kg) are expressed as mean ± S.E. of percentages of values at 0 min. Data from sham-operated and denervated rats are shown. ANOVA results of sinoaortic denervation on BAT-SNA to AVP for 120 min: AVP-denervated rats *vs.* AVP-sham operated rats, $P < 0.05$; saline -denervated rats *vs.* saline -sham operated rats, $P > 0.05$.

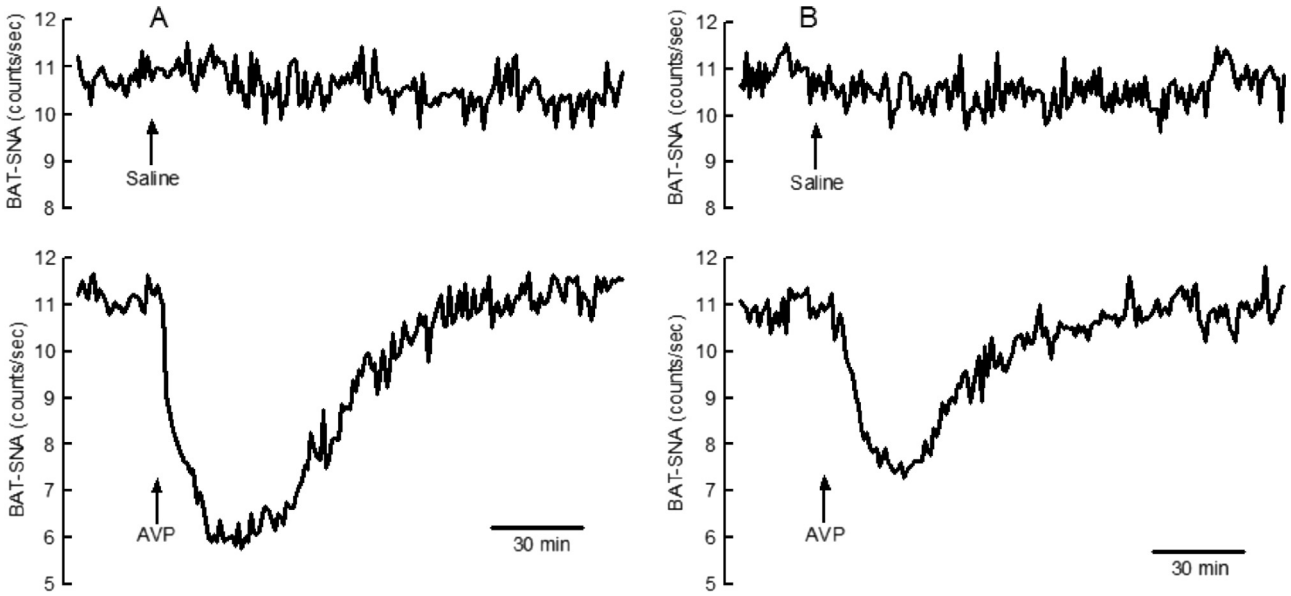

Fig. 5. The typical recordings of BAT sympathetic nerve activity (BAT-SNA) in sham-operated (A) and denervated rat (B) after the intraperitoneal injection of saline (1 ml/kg) or AVP (10 μg/kg).

AVP was similar to that of core temperature, but the decreases in BAT temperature preceded the decreases in core temperature, and the recovery from hypothermic responses in BAT temperature was more rapid compared with core temperature. This would suggest that AVP suppression of BAT thermogenesis could play an important role in AVP-induced hypothermia in rats (Yang et al., 2013). On the other hand, experimental results also show that the mean BAT temperature was lower than core temperature; these lower values could be explained by the fact that BAT is located under the skin and measuring its temperature is a little bit tricky because it is in a cooler region of the body and not in the true core of the animal. Our previous studies compared BAT temperature with axillary temperature using radio-telemetry, the experiment demonstrated that temperature probes are both being positioned under the skin but the BAT temperature probe is obviously showing much warmer temperature compared to axillary temperature (Yang et al., 2012).

The preoptic area (POA) plays a critical role in the precise regulation of body temperature, and it has been suggested that POA warm-sensitive neurons facilitate heat loss responses and inhibit heat production responses, whereas cold-sensitive neurons might have the opposite roles (Chen et al., 1998; Zhao and Boulant, 2005; Nakamura and Morrison, 2008; Tan et al., 2016). During studies on the mechanism of the hypothermic effects of AVP in rats, we found that AVP increases the firing rates of warm-sensitive neurons, while decreasing the firing rates of cold-sensitive neurons in the POA (Yang and Chen, 1994; Tang et al., 2012). These changes are due to the AVP enhancing the rise rate of depolarization prepotential in warm-sensitive neurons and reducing it in cold sensitive neurons (Tang et al., 2012). In addition, the physiological range of circulating AVP is sufficient to facilitate the baroreflex (Oikawa et al., 2007). Shido et al. (1984) assumed that the hypothermic effects of peripheral injection of AVP could be attributed to the sinoaortic baroreflex suppression of nonshivering thermogenesis, but BAT temperature was not measured in these experiments. Thus, we examined the effect of sinoaortic denervation on AVP-induced hypothermia in rats, and demonstrated that sinoaortic denervation attenuated the suppressive effects of intraperitoneal injection of AVP on core and BAT temperatures (Figs. 1 and 2). These results suggest that the sinoaortic baroreceptors are involved in the suppressive effects of AVP on core and BAT temperatures. It must be pointed out, however, our data were obtained from simultaneous measurement of core and BAT temperatures in the same animal by dual probe telemetric monitoring transmitters.

BAT is specialized for the process of nonshivering thermogenesis, where oxidative metabolism is uncoupled from ATP production and, in the process, energy is expended. This tissue is thermogenic by increasing the metabolic rate (Tansey and Johnson, 2015; Morrison, 2016). Sympathetic nervous system activity, in response to inputs from peripheral and central thermoreceptors, can stimulate BAT thermogenesis (Tansey and Johnson, 2015). Increases in BAT sympathetic nerve activity lead to the release of norepinephrine from postganglionic nerve terminals thereby stimulating brown adipocyte β3-adrenoceptors that ultimately activate uncoupling protein-1 resulting in thermogenesis increases (Ryu et al., 2015; Morrison, 2016). In addition, BAT thermogenesis can be modulated by a number of nonthermal factors, including hormonal signals, hypoxia, infection, hypoglycemia, and psychological stress (Morrison and Madden, 2014). However, the effects of peripheral administration of AVP on BAT sympathetic nerve activity were not evaluated. In this study we examined effect of AVP on BAT sympathetic nerve activity. The experimental results show that peripheral administration of AVP significantly suppressed BAT sympathetic nerve activity in rats. Interestingly, the duration of the suppressive effects in BAT sympathetic nerve activity following AVP was similar to that the hypothermic responses of core and BAT temperatures, but also the greatest level of suppression occurring time was also similar. This would suggest that the hypothermic effect of peripheral injection of AVP was produced by a reduction of BAT thermogenesis through the suppressing BAT sympathetic nerve activity.

Although blood pressure was not measured in this study, we can assume that blood pressure was elevated by approximately 30 mmHg at the time of the peak hypothermic effect of AVP treatment (Shido et al., 1984; Paro et al., 2003). Decreases in core and BAT temperatures were preceded by an elevation of aortic blood pressure, and were related to the dosage of AVP administered (Shido et al., 1984; Yang et al., 2013). Therefore, it can be said that the hypertension resulting from peripheral AVP caused a suppression in BAT thermogenesis via activation of the sinoaortic baroreceptors (Shido et al., 1984; Rascher et al., 1981; Pires et al., 2013).

To determine the mechanisms of suppressive effects of peripheral administration of AVP on BAT sympathetic nerve activity and BAT temperature, we noted that the AVP plays an important role in the modulation of the baroreflex (Oikawa et al., 2007). Moreover, it is thought that arterial baroreceptor reflex control of sympathetic nerve activity could affect core and skin temperatures through chemical thermogenesis (Zhang et al., 2003). In fact, there is evidence showing that stimulation of baroreceptors modulates heat loss through the tail (Zhang et al., 2003; Pires et al., 2010). Thus, we tested effects of AVP on BAT sympathetic nerve activity in sinoaortic denervation rats, and found that sinoaortic denervation attenuated the suppressive effects of intraperitoneal injection of AVP on BAT sympathetic nerve activity (Figs. 5 and 6). These findings suggest that the sinoaortic baroreceptor reflex might be involved in suppressive effects of peripheral administration of AVP on BAT sympathetic nerve activity and BAT thermogenesis.

5. Conclusion

We previously demonstrated that peripheral AVP-induced hypothermia attributed to the suppression of thermoregulatory heat production (i.e., a reduction of BAT thermogenesis) and the increase of saliva spreading for evaporative heat loss (i.e., grooming behavior) (Yang et al., 2013). The present study suggests that intraperitoneal injection of AVP rapidly decreased BAT sympathetic nerve activity and BAT temperature. Furthermore, we found that sinoaortic denervation attenuated the suppressive effects of peripheral administration of AVP on BAT sympathetic nerve activity, core and BAT temperatures. Therefore, these results indicate that the hypothermic effects of peripheral administration of AVP are partially mediated by the arterial baroreceptor reflex suppression of BAT sympathetic nerve activity and BAT thermogenesis.

Acknowledgements

This work was supported by grants from National Natural Science Foundation of China (No. 30870901).

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