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Arginine vasopressin does not mediate heat loss in the tail of the rat

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ABSTRACT

It has been reported that hypothermia induced by arginine vasopressin (AVP) is brought about by a coordinated response of reduced thermogenesis in brown adipose tissue (BAT) and increased heat loss through the tail of rats. However, it is well known that AVP is one of the strongest peripheral vasoconstrictors. Whether the AVP-induced hypothermia is associated with an increase in heat loss through the tail is questionable. Therefore, the present study assessed the relationship between the effects of AVP on tail skin temperature and the induced hypothermic response, and to determine if peripheral AVP administration increases heat loss from the tail. Core, BAT and tail skin temperature were monitored by telemetry in male Sprague–Dawley rats before and after intraperitoneal administration of AVP or vasopressin receptor antagonist. We also analyzed simultaneously of the time-course of AVP-induced hypothermic response and its relationship with changes in BAT temperature, and effect of AVP on grooming behavior. The key observations in this study were: (1) rats dosed with AVP induced a decrease in heat production (i.e., a reduction of BAT thermogenesis) and an increase of saliva spreading for evaporative heat loss (i.e., grooming behavior); (2) AVP caused a marked decrease in tail skin temperature and this effect was prevented by the peripheral administration of the vasopressin V1a receptor antagonist, suggesting that exogenous AVP does not increase heat loss in the tail of rats; (3) the vasopressin V1a receptor antagonist could elevate core temperature without affecting tail skin temperature, suggesting that endogenous AVP is involved in suppression of thermogenesis, but not mediates heat loss in the tail of rats. Overall, the present study does not support the conclusion of previous reports that AVP increased tail heat loss in rats, because AVP-induced hypothermia in the rat is accompanied by a decrease in tail skin temperature. The data indicate that exogenous AVP-induced hypothermia attributed to the suppression of thermoregulatory heat production and the increase of saliva spreading for evaporative heat loss.

1. Introduction

It has been reported that the arginine vasopressin (AVP) plays an important role in normal thermoregulation. A number of studies have demonstrated that intracerebroventricular administration of high doses of AVP could cause hypothermia at normal body temperatures (Drago et al., 1997; Steiner et al., 1998; Pittman et al., 1998). Peripheral administration of AVP also causes a reduction in normal body temperature, whereas vasopressin V_1 receptor antagonist leads to an elevation in temperature (Steiner et al., 1998; Yang et al., 2012). We found that AVP is involved in mediating the hypothermic effects of chlorpyrifos (an organophosphate insecticide) in male and female rats, because chlorpyrifos can increase plasma AVP and vasopressin V_1 receptor antagonist attenuated the hypothermia effect of anti-ChE agents (Yang and Gordon, 2002).

Some studies have assessed the mechanism by which AVP evokes the hypothermia. Evidence suggests that hypothermia induced by AVP is brought about by a coordinated response of reduced thermogenesis in brown adipose tissue (BAT) and increased heat loss through the tail (Kruk and Brittain, 1972; Wilkinson and Kasting, 1987; Paro et al., 2003). The authors therefore conclude that AVP elicits hypothermia by reducing the thermoregulatory set point (Wilkinson and Kasting, 1987; Kasting, 1989; Bicego-Nahas et al., 2000).

In addition, it is well known that AVP is a strong peripheral vasoconstrictor (Dünser et al., 2003; Friesenecker et al., 2006). When blood vessels constrict, the flow of blood is restricted or decreased, thus, retaining body heat. The question is whether the AVP-induced hypothermia is related to an increase in heat loss

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through the tail? Previous studies were performed using the thermistors. Tail skin temperature was typically monitored by attaching thermistors to the external surface of the tail (Kruk and Brittain, 1972; Wilkinson and Kasting, 1987; Paro et al., 2003). These methods introduced stress-related temperature changes due to animal handling on the day of study that may lead to data artifacts and misinterpretation (Dallmann et al., 2006; Sharp et al., 2003).

The tail of the rat is a crucial site for the regulation of heat loss (Gordon et al., 2002). Therefore, the present study was first to measure tail skin temperature and core temperature by telemetric monitoring transmitter, and to assess the relationship between the effects of peripheral AVP administration (using several different doses) on heat loss from the tail in the rat and the induced hypothermic response. Subsequently, we analyzed simultaneously the time-course of AVP-induced hypothermic response and its relationship with changes in BAT temperature, and effect of AVP on grooming behavior.

2. Materials and methods

2.1. Animals and drugs

Adult male Sprague–Dawley rats weighting 220–320 g were used for all experiments (Institute of Laboratory Animal Sciences, Sichuan Academy of Medical Sciences, China). Rats were housed individually in acrylic cages lined with wood shavings, maintained at an ambient temperature of 22 °C, and exposed to a daily 12:12 light: dark photoperiod (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 and vasopressin V1a receptor antagonist [beta-Mercapto-beta, beta-cycloentame-thylenepropionyl (1), O–Me–Tyr (2), Arg (8)]–VP were purchased from Sigma Chemical Co. (St Louis, MO). The drugs were dissolved in pyrogen-free sterile saline.

2.2. Surgery

Rats were anesthetized with sodium pentobarbital (40 mg/kg, i.p.). The fur on the abdomen (implantation site) and interscapular area were clipped and the skin disinfected with Povidone-Iodine Solution and 70% ethanol. A 2–3 cm skin incision was made in the midline of the abdomen and extended through the abdominal musculature. A small incision was also made in the midline of scapular region. The dual probe transmitters (Data Sciences International, Model TL10M2-F40-TT) 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 (Yang et al., 2012). The abdominal muscle incision was sutured and the skin was closed with wound clips. The interscapular muscle incision and the skin were closed with sutures. Following surgery, rats were administered a penicillin antibiotic (20,000 units; intramuscularly). The rats were allowed at least 7 days of recovery before testing.

2.3. Measurement of core and BAT temperature

Core and BAT temperature were monitored in undisturbed rats using radiotelemetry (Data Sciences International, St. Paul, MN, USA). 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.

2.4. Measurement of tail skin temperature

Tail skin temperature was monitored at 5 min intervals in undisturbed rats using radiotelemetry (Data Sciences International, St. Paul, MN, USA). Details of the telemetry system have been published (Gordon et al., 2002). Briefly, tail skin temperature was measured noninvasively with radiotelemetric transmitters (Data Sciences, model TA10TA-F20) placed on the dorsal side of the tail and held in place with a guard that served to keep the transmitter in place on the tail and prevent the rat from chewing on the transmitter. The guard was positioned about 1.5 cm from the base of the tail.

Tail and core temperature were used to calculate the heat loss index (HLI). HLI was calculated according to the formula

$$\mathrm{HLI} = (T_{sk} - T_a)/(T_c - T_a)$$

HLI eliminates the passive effects of ambient temperature (T_a) and core temperature (T_c) on tail skin temperature (T_{sk}). The HLI is essentially a measure of the active, nonevaporative heat exchange attributed to peripheral vasomotor mechanisms. The value of HLI will vary from 0 to 1.0, representing states of fully vasoconstriction to fully vasodilation, respectively.

To compare the radiotelemetric transmitters with the thermistors, Tail skin temperature was also measured at 15 min intervals by using a thermistor in rats maintained at an ambient temperature of 22 °C. A thermistor probe was taped to the dorsal side of the rat's tail and positioned approximately 1.5 cm from the base of the tail. The temperature from the thermistor probe was measured with a digital meter (SN2202, Beijing Sinan Instrument, China). Its precision and accuracy were ±0.1 °C.

2.5. Grooming behavior measures (behavioral test)

The grooming behavior was recorded as described previously (Drago et al., 1997). Rats were placed individually in the home cage [45×30×20 cm (length×width×depth)] in order to avoid grooming due to a novel environment. The grooming behavior of the rats was sampled every 15 s. The occurrence of the following single elements of grooming was scored as grooming: face washing (movement of forepaws across snout, eyes and/or ears), body grooming (licking body fur and tail). The mean score of the three observations was used for the statistical analysis.

2.6. Experimental protocol

In all experimental protocols, the environmental chamber was set at 22 °C. The rats were placed in clean cages with wood shavings at 16:00 h. The rats were allowed to adapt to the chamber overnight. The following day the rats were administered intraperitoneally with the AVP (1, 5, and 10 μg/kg) or vasopressin V1a receptor antagonist (30 μg/kg) at 10:00 h. Saline (1 ml/kg) was used for control rat injection, at the same volume. Core, BAT, and tail skin temperature of the rat were monitored by radio telemetry for at least 6 h prior to administration.

In order to further determine the effect of AVP on core and tail skin temperature, rats received AVP (10 μg/kg) or saline, followed immediately by an injection of vasopressin V1a receptor antagonist (30 μg/kg) or saline at 10:00 h. Saline (1 ml/kg) was used for control rat injections.

The rats were allowed to recover for at least 10 days and then they were retested using a crossover design where the rats received AVP or vasopressin V1a receptor antagonist were given

saline, and the rats received saline were given AVP or vasopressin V1a receptor antagonist.

2.7. Statistical analysis

The telemetry parameters were monitored at 5 min intervals from rats housed individually in the animal facility. Data were plotted as mean ±S.E. Values of core, BAT, and tail skin temperature are the changes from basal values. Data were analyzed statistically by ANOVA followed by multi-range (or others) test to assess differences between groups. Core temperature 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 core temperature for drugs. Values of $P<0.05$ were considered to be significantly different.

3. Results

3.1. AVP-induced hypothermic response and changes in tail skin temperature

In all experimental protocols, core temperature ranged from 36.88±0.22 °C (mean±S.E.) to 37.06±0.26 °C during the control period, and tail skin temperature ranged from 28.90±0.32 °C to 30.25±0.44 °C. No difference in initial core temperature or tail skin temperature values was observed among the different groups (Figs. 1 and 2). Administration of the saline led to a transient elevation in core temperature (Fig. 1A) and reduction in tail skin temperature (Fig. 2A) that was attributed to the stress of handling and injection procedure, because restrained rats reduce heat loss and increase heat production (Gordon et al., 2002).

Administering 1, 5 or 10 μg/kg AVP led to dose-related reductions in core temperature (Fig. 1). Core temperature reached a nadir at 35 min after treatment. Rats treated with 1 μg/kg of AVP underwent a significant drop in core temperature, reaching a nadir of 0.73±0.12 °C below control levels after administration. The maximum decrease in core temperature following dosing of 5 and 10 μg/kg of AVP was −1.36±0.15 °C and −1.52±0.14 °C, respectively.

It is interesting to note that the rats administered with AVP (1, 5 or 10 μg/kg) also induced a prompt, marked decrease in tail skin temperature in a dose-related manner (Fig. 2). Rats administered with 1 μg/kg AVP underwent a 1.85±0.17 °C reduction in tail skin temperature 60 min after administration (Fig. 2B). Rats administered 5 and 10 μg/kg AVP underwent 2.58±0.19 °C and 3.55±0.23 °C reductions in tail skin temperature within 60 min (Fig. 2C and D), respectively.

In addition, AVP-induced hypothermia occurs concomitantly when the ear skin becomes pale and white. The skin pallor response on the ear lasted for 15–18 min before returning to their baseline skin color.

Conversion of the tail and core temperature data to heat loss index (HLI) illustrates the marked decrease in heat loss from the tail in rats treated with AVP (Fig. 3). In rats received 1 μg/kg AVP, HLI was reduced by over 0.12 units at 45 min after treatment. In animals that received 5 and 10 μg/kg AVP, HLI was reduced by over 0.18 and 0.22 units at 60 min after treatment, respectively. HLI was not markedly altered following intraperitoneal injection of saline.

However, results from the thermistors are inconsistent with radiotelemetric transmitters. Results obtained by use of the thermistor were: (1) tail skin temperature increased by 0.33±0.10 °C and 0.44±0.13 °C following dosing with 5 and 10 μg/kg AVP, respectively; (2) did not measure a significant difference in tail skin temperature and a transient reduction in tail skin temperature following dosing with 1 μg/kg AVP or saline (Fig. 4).

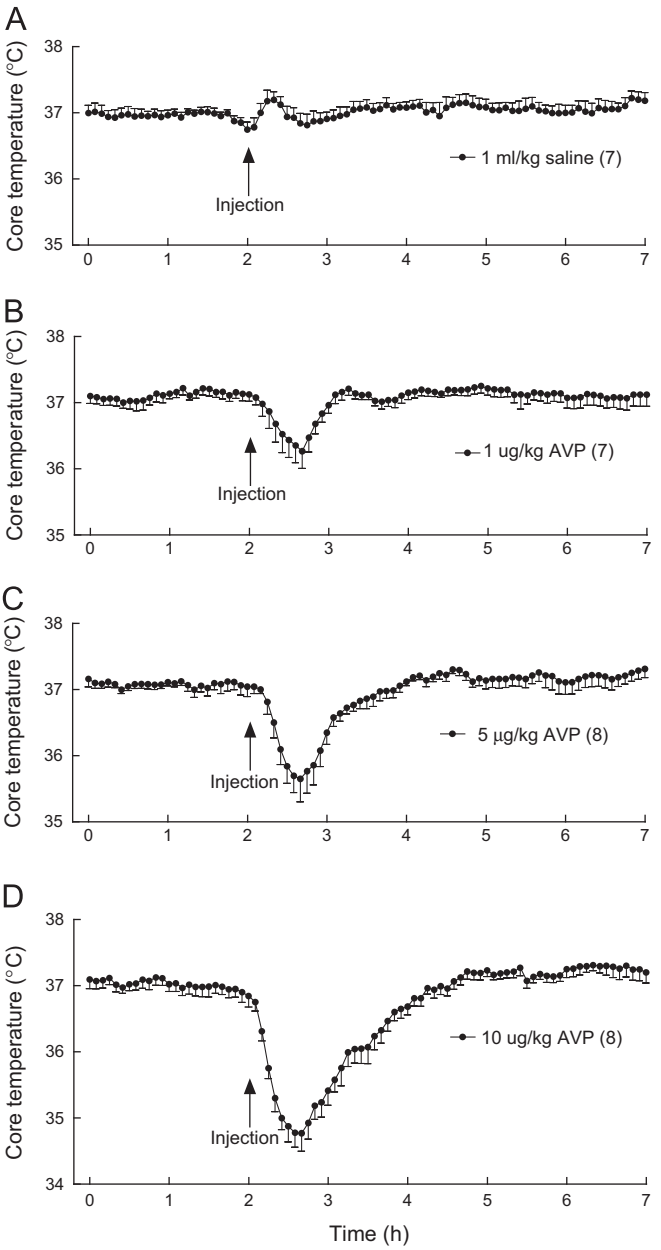

Fig. 1. Effect of intraperitoneal injection of different doses of AVP (1, 5 or 10 μg/kg) on core temperature. Data were plotted as mean±S.E. In all figures, numbers in parenthesis indicate sample size. ANOVA analysis for saline comparing effects of 1 μg/kg AVP for 60 min: core temperature (treatment, $p<0.05$; treatment-time, $p<0.05$). ANOVA results of 5 and 10 μg/kg AVP for 90 min: core temperature (treatment, $p<0.005$; treatment-time, $p<0.005$).

3.2. Effect of vasopressin V1a receptor antagonist on core and tail skin temperature

Immediately following injection of saline and vasopressin V1a receptor antagonist there was a stress-mediated rise in core temperature lasting 70 min that is attributed to the handling and injection procedure (Fig. 5). In addition, there was an abrupt decrease in tail skin temperature following injection of saline and vasopressin V1a receptor antagonist.

The rats dose with 30 μg/kg vasopressin V1a receptor antagonist led to a significant increase in core temperature that persisted for over 8 h (Fig. 5A).The core temperature was 0.30±0.11 °C higher than that of the rats given saline ($p<0.05$); however, tail skin

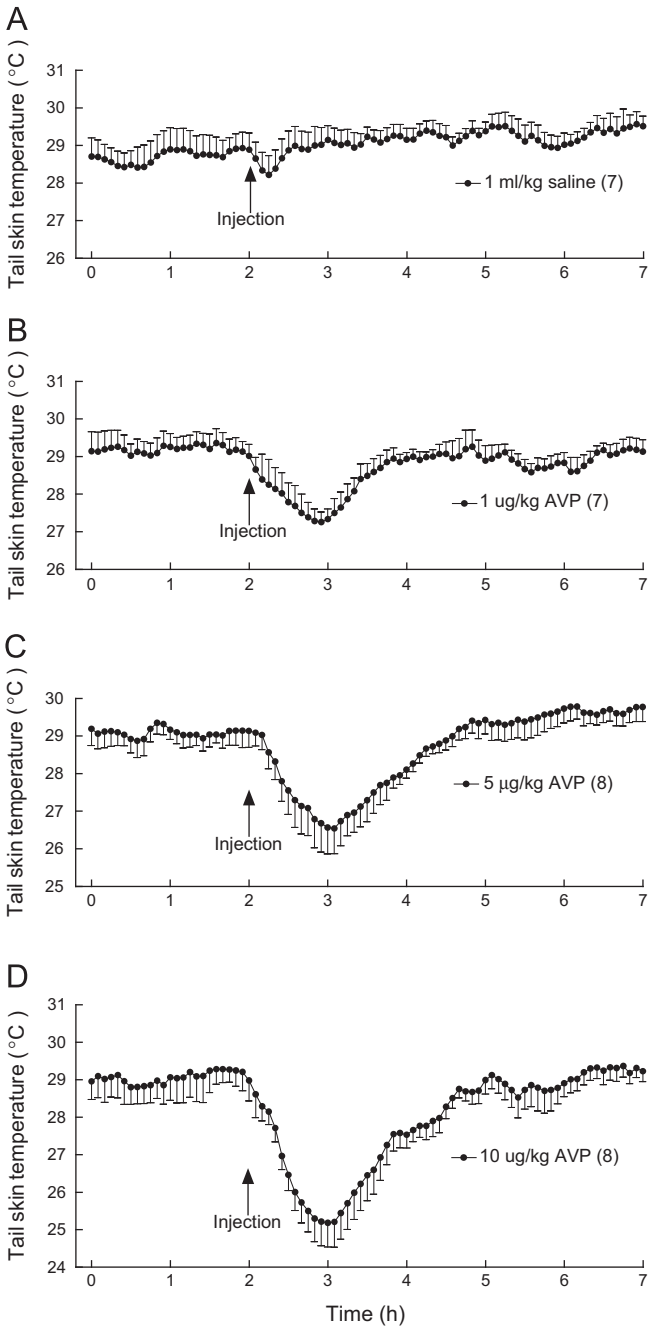

Fig. 2. Effect of intraperitoneal injection of different doses of AVP(1, 5 or 10 μg/kg) on tail skin temperature. ANOVA analysis for saline comparing effects of 1 μg/kg AVP for 60 min: tail skin temperature (treatment, $p<0.005$; treatment-time, $p<0.005$). ANOVA results of 5 and 10 μg/kg AVP for 90 min: tail skin temperature (treatment, $p<0.001$; treatment-time, $p<0.001$).

temperature was slightly, but not significantly, higher than that of saline rats (Fig. 5B).

3.3. Effect of vasopressin V1a receptor antagonist on core and tail skin temperature after treatment with AVP

Fig. 6 shows the effect of vasopressin V1a receptor antagonist on core and tail skin temperature after treatment with AVP. Intraperitoneal injection of the vasopressin V1a receptor antagonist (30 μg/kg) prevented the decrease in tail skin temperature induced by AVP (10 μg/kg) and its hypothermic effect.

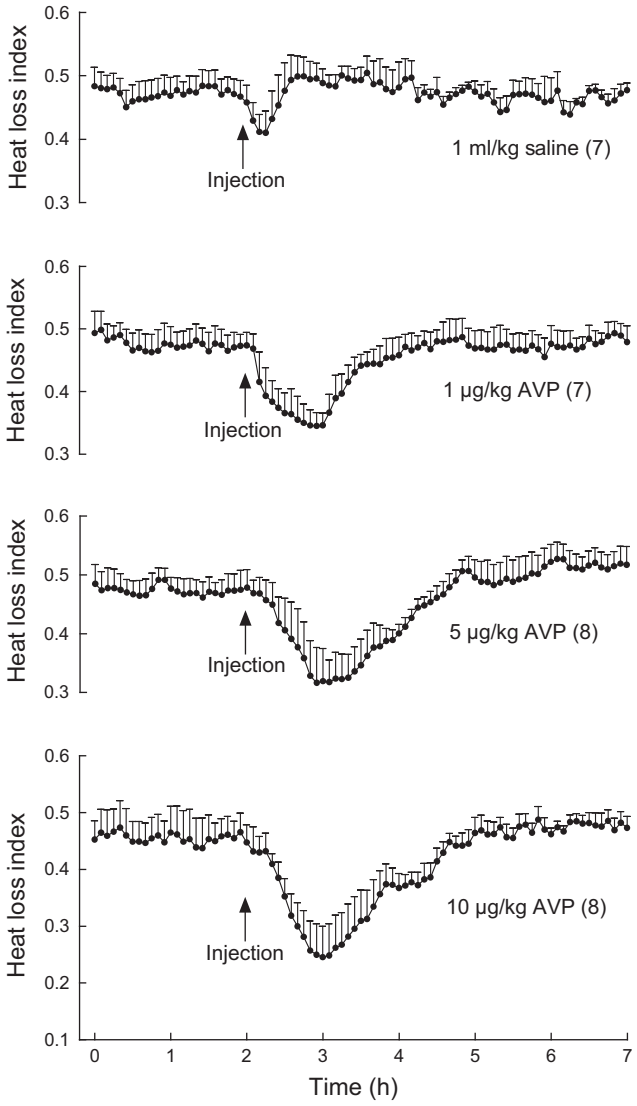

Fig. 3. Time-course of heat loss index (HLI) of rats treated the saline or AVP. Data plotted as mean±S.E. HLI calculated from tail skin and core temperature data in the Figs. 1 and 2 (see Section 2). ANOVA results of 1, 5 or 10 μg/kg AVP for 90 min: $p<0.01$, significant difference compared to saline group.

3.4. AVP-induced hypothermic response and its relationship with the change in BAT temperature

Fig. 7 shows that time course of core and BAT temperature was simultaneously measured in undisturbed rats using dual probe transmitter's temperature probe. Administration of saline led to a transient elevation in core and BAT temperature that was attributed to the handling and injection procedure (Fig. 7A). Approximately 50 min after administration of saline, core and BAT temperature returned to near baseline levels.

At 10:00 h administration with 10 μg/kg AVP led to a significant decrease in core temperature that persisted for over 90 min. The mean core temperature was 2.10±0.13 °C lower than that of the rats given saline ($p<0.001$). At the same time, the mean BAT temperature was 1.95±0.18 °C lower than control group (Fig. 7B, $p<0.001$). The amplitude of the hypothermic response in BAT temperature following AVP was similar to that of core temperature. It was noted that the duration of the hypothermic response in BAT temperature was shorter than corresponding core temperature (Fig. 7B). The recovery from AVP-induced hypothermic responses

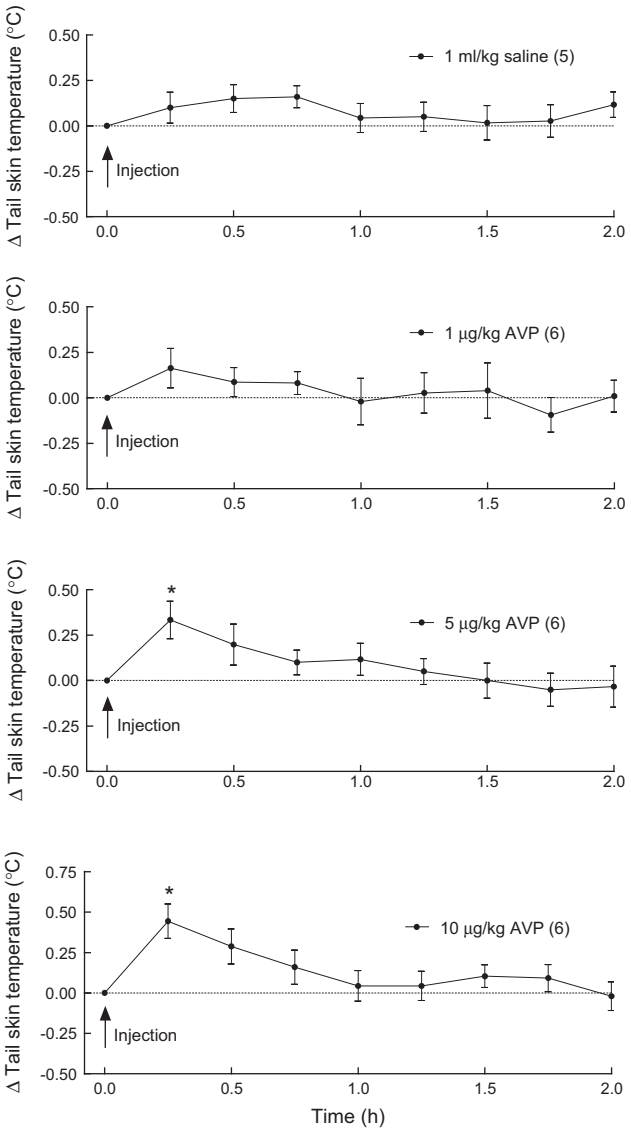

Fig. 4. Change in tail skin temperature after intraperitoneal administration of 10 μg/kg AVP in rats using a thermistor. *$p<0.05$, significant difference compared to saline group.

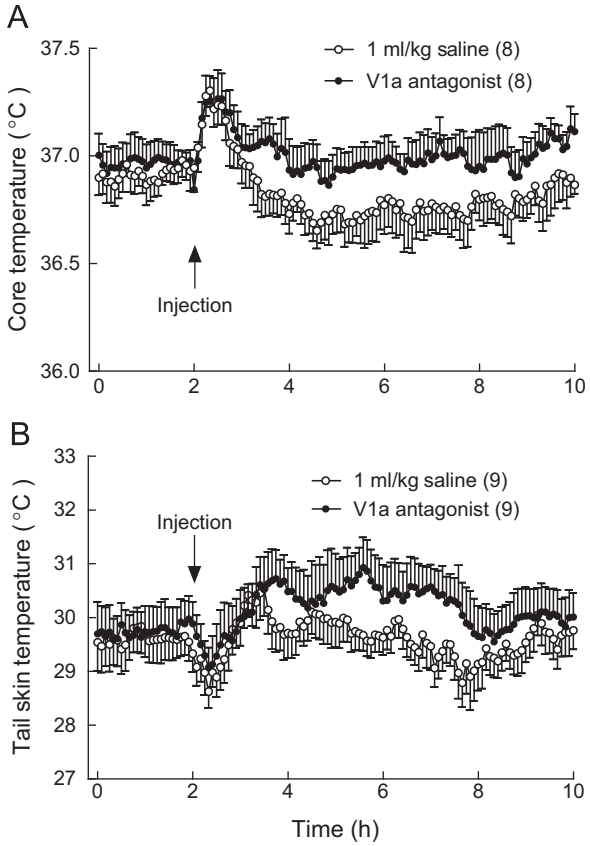

Fig. 5. Effect of intraperitoneal administration of saline or 30 μg/kg vasopressin V1a receptor antagonist on core and tail skin temperature. ANOVA analysis for saline comparing effects of vasopressin V1a receptor antagonist treatment for 8 h: core temperature (treatment, $p<0.05$; treatment-time, $p<0.05$); tail skin temperature (not significant).

in BAT was more rapid compared with core temperature (Fig. 8B), suggesting that AVP is involved in suppression of BAT thermogenesis.

3.5. Effect of AVP treatment on grooming behavior

Grooming activity, including face washing and body grooming (licking body fur and tail), was increased markedly at 40 min after AVP ($P<0.01$ vs. saline group) whereas saline had no effect. Approximately 60 min after administration, grooming activity of the AVP group retuned to near baseline levels. The vasopressin V1a receptor antagonist completely prevented the behavioral effect of vasopressin, but the vasopressin V1a receptor antagonist had no effect on grooming activity in the saline-treated rats (Table 1).

4. Discussion

The present study provides evidence that peripheral injection of AVP can elicit hypothermia in the rat, but also induce a rapid decrease in heat loss through the tail. This is supported by the following two new key findings: (1) AVP-induced hypothermia in the rat is accompanied by a decrease in tail skin temperature and (2) intraperitoneal injection of the vasopressin V1a receptor antagonist prevented the decrease in tail skin temperature induced by AVP and its hypothermic effect. Experimental results also show that endogenous AVP does not mediate heat loss in the tail of the rat, because vasopressin V1a receptor antagonist may cause a slight increase in tail skin temperature, but the change was not significant.

Previous studies have suggested that AVP plays an important role in thermoregulation, because intracerebroventricular and peripheral administration of AVP may elicit hypothermia (Drago et al., 1997; Steiner et al., 1998; Pittman et al., 1998). Hyperthermia can be elicited in rats by cooling of the preoptic area, which results in a vigorous metabolic response. In such animals, infusion of AVP into the lateral septum completely suppresses the metabolic response and hyperthermia (Pittman et al., 1998). Recent studies found that endogenous AVP is involved in the circadian changes of core temperature (Li et al., 2009; Yang et al., 2012). In addition, it has been reported that AVP evokes a drop in core temperature by a coordinated process that includes not only a reduction in BAT temperature (Wilkinson and Kasting, 1987; Paro et al., 2003; Yang et al., 2012) but also an increase in heat loss through the tail (Kruk and Brittain, 1972; Wilkinson and Kasting, 1987; Paro et al., 2003).

However, AVP is a potent endogenous vasopressor hormone and one of the strongest vasoconstrictors in the skin (Dünser et al., 2003; Friesenecker et al., 2006). The clinical use of AVP has been shown to produce severe ischemia of the skin and limbs (Dünser et al., 2003). Animal experiments also show that AVP can reduce arteriolar diameter and microvascular flow, significantly decreased functional capillary density (Friesenecker et al., 2004; Friesenecker et al., 2006).

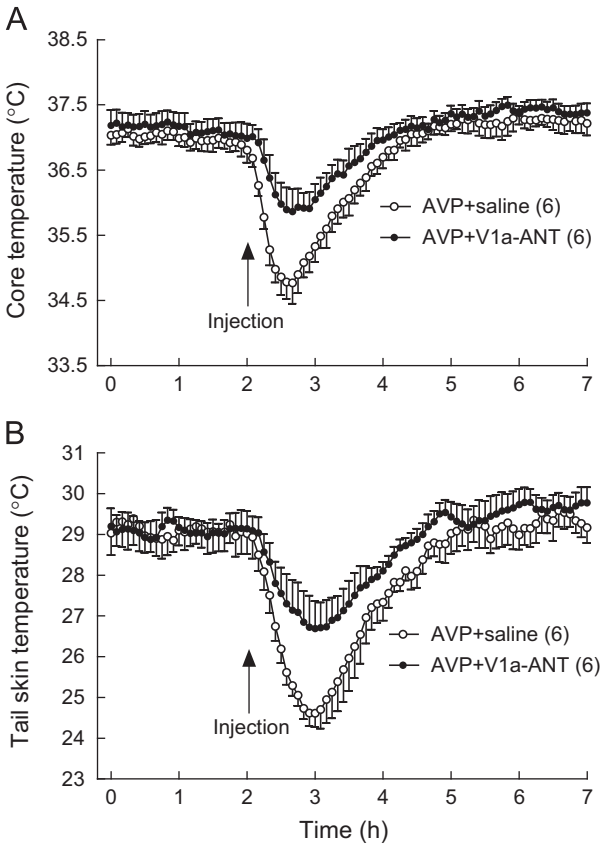

Fig. 6. Effect of intraperitoneal administration of saline or 30 μg/kg vasopressin V1a receptor antagonist (V1a-ANT) on core (A) and tail skin temperature (B) after treatment with saline or 10 μg/kg AVP. ANOVA analysis for AVP/saline comparing effects of AVP/V1a-ANT for 90 min: core temperature (treatment, $p<0.01$; treatment-time, $p<0.01$); tail skin temperature (treatment, $p<0.01$; treatment-time, $p<0.01$).

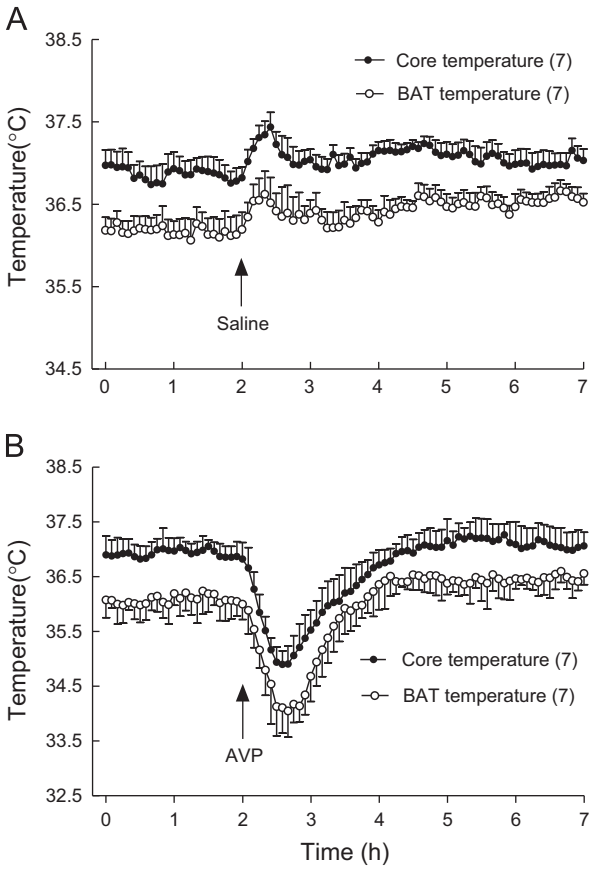

Fig. 7. Simultaneous telemetric monitoring of the time course for effect of AVP on core and BAT temperature in rats. One-way analysis for saline comparing effects of AVP treatment for 90 min: core temperature (treatment, $p<0.01$; treatment-time, $p<0.01$); BAT temperature (treatment, $p<0.01$; treatment time, $p<0.01$). In the figure, each point represents the mean of all temperatures recorded simultaneously at 5 min intervals.

Considering the evidence that AVP has the strongest vasoconstrictive effect, we first assessed the relationship between the effects of peripheral AVP administration on the tail skin temperature in undisturbed rats and it induced hypothermic response. The experimental results showed that intraperitoneal injection of AVP caused a dose-related decreased hypothermic response. One surprising finding of the study was that rats administered with AVP also induced a prompt, marked decrease in tail skin temperature in a dose-related manner, indicating that AVP-induced vasoconstriction leads to decreases in blood flow through the tail. Although blood flow in the tail was not measured in this study, we can assume that systemic vasoconstriction caused blood-flow velocity index in the tail to decrease by 88.7% after AVP treatment (Wienzek et al., 2007). In further experiments, we examined the effect of vasopressin V1a receptor antagonist on core and tail skin temperature after treatment with AVP, because the physiologic effects of AVP are mediated by V_1 receptors (Richmond, 2003; Li et al., 2009). The decreases of core and tail skin temperature were found after intraperitoneal injection of AVP and this effect were prevented by the peripheral administration of the vasopressin V1a receptor antagonist. The results of this study strongly suggest that exogenous AVP does not increase heat loss in the tail of the rat, because peripheral AVP-induced hypothermia in rats is accompanied by a decrease in tail skin temperature.

Endogenous AVP, acting through V1a receptor, could be involved in tonic thermoregulatory processes (Steiner et al, 1998; Yang and Gordon, 2002; Yang et al, 2012). Therefore, we also examined the effect of vasopressin V1a receptor antagonist on normal core temperature and tail skin temperature in rats. Intraperitoneal administration of vasopressin V1a receptor antagonist led to a significant elevation in normal core temperature that persisted for over 8 h, whereas tail skin temperature was slightly, but not significantly, higher than that of saline rats. The vasopressin V1a receptor antagonist could elevate core temperature without affecting tail skin temperature, suggesting that endogenous AVP is involved in suppression of thermogenesis, but not mediates heat loss in the tail of the rat.

It must be pointed out, however, our data were obtained from a noninvasive telemetric probe technique to measure tail skin temperature in undisturbed rats. The probe provides continuous temperature measurements of the surface of the rat's tail (Gordon et al., 2002).

To compare the radiotelemetric transmitters with the thermistors, tail skin temperature was also measured by using the thermistor in rats. An increase in tail skin temperature was observed following administration of AVP (5 or 10 μg/kg). The measurement results from the thermistors are consistent with previous studies (Kruk and Brittain,1972; Wilkinson and Kasting,1987; Paro et al., 2003). This result is difficult to interprete, as AVP-induced vasoconstriction leads to decreases in blood flow through the tail (Dünser et al., 2003; Wienzek et al., 2007). One possibility is that repeated handling induces stress-related temperature changes that may lead to data artifacts and misinterpretation (Dallmann et al., 2006; Sharp et al., 2003).

Several studies have reported that peripheral administration of AVP induced hypothermia by reduced thermogenesis in BAT (Paro et al., 2003; Yang et al., 2012). The changes in BAT temperature

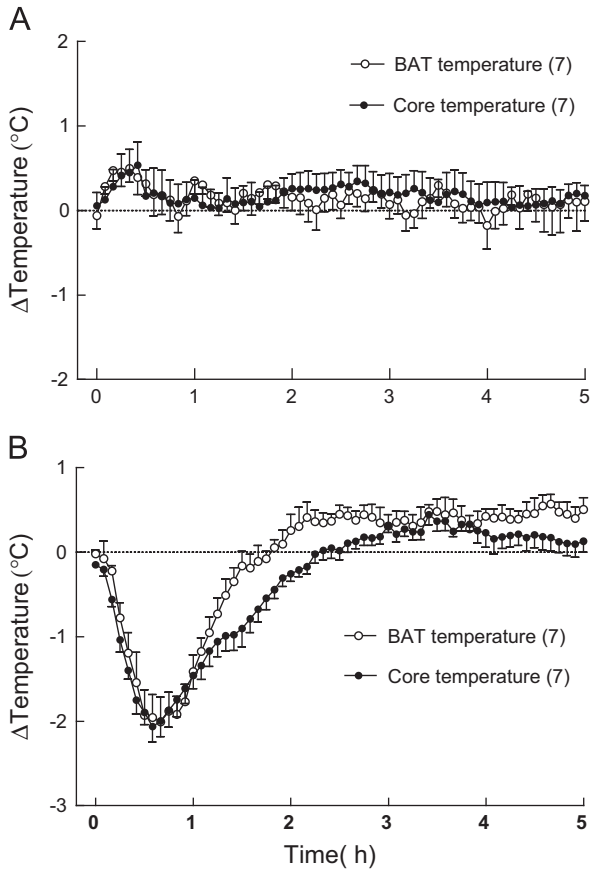

Fig. 8. Time-course of the changes in core and BAT temperature following intraperitoneal administration of saline (A) or AVP (B). Temperature changes were calculated from data measured at the time of injection (see Fig. 7).

Table 1
Effects of intraperitoneal injection of arginine vasopressin(AVP) and vasopressin V1a receptor antagonist (V1a-ANT) on grooming activities in rats (counts/15 s, $\bar{x}$±S.D.).

groups	Before administration	Time After intraperitoneal injection (min)		
		20	40	60
Saline+saline (7)	5.75±0.75	6.25±0.83	6.11±0.92	5.36±0.72
Saline +V1a-ANT(6)	4.83±0.86	5.73+1.3	5.56+0.89	5.08+0.66
AVP+saline (7)	5.17±0.68	6.17±0.98	26.80±4.08**	10.63±1.53*
AVP+V1a-ANT(6)	6.23+0.82	7.3 4±1.31	8.43±1.15	7.55±0.97

The number in parentheses indicates the number of animals per each group.
* $P<0.05$,
** $P<0.01$ vs saline group.

could 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). However, previous studies were performed using the single probe transmitters, core and BAT temperature could not be simultaneously measured telemetrically within the same animal. In the present study, our data were obtained from simultaneous measurement of core and BAT temperature in the same animal by dual probe telemetric monitoring transmitters. Interestingly, the amplitude of the hypothermic response in BAT temperature following AVP was similar to that of core temperature, but 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.

Because rodents neither sweat nor pant, they rely on increased salivary secretion and saliva spreading for evaporative heat loss (Gordon, 2005; Morrison and Nakamura, 2011). Saliva grooming and sweating achieve the same result of moistening skin to increase evaporative water loss. Normal grooming behavior accounts for about 7–8% of the total water loss by evaporation in rats maintained at room temperature (Gordon, 2005). It has been reported that intracerebroventricular administration of AVP induced hypothermia and enhanced grooming behavior (Drago et al., 1997; Lumley et al., 2001). The authors concluded that the preoptic area is one site in which AVP induces grooming behavior (Lumley et al., 2001). In this study, intraperitoneal injection of AVP can also enhance grooming behavior and this effect was prevented by the peripheral administration of the vasopressin V1a receptor antagonist, suggesting that peripheral AVP-enhanced grooming behavior could play a role in AVP-induced hypothermia, and peripheral AVP could mediate evaporative heat loss in the rat.

5. Conclusion

The present study does not support the conclusion of previous reports that AVP elicits hypothermia by increasing heat loss through the tail, because the rats administered with AVP underwent a marked decrease in tail skin temperature. Administration of Vasopressin V1 receptor antagonist also indicated that endogenous AVP does not mediate heat loss in the tail of the rat. Overall, the data indicate 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).

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