SHORT COMMUNICATION

ANXIOLYTIC DRUGS INHIBIT HYPERTHERMIA INDUCED BY HANDLING IN FARMED SILVER FOXES (*VULPES VULPES*)

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Abstract *Animal Welfare 1998, 7:* 97-100

As a contribution to the ongoing work aiming to improve welfare in farmed silver foxes (Vulpes vulpes), *the present study attempted to investigate stress-induced hyperthermia (SIH) as a physiological indicator of fear or anxiety in this species. Measuring rectal temperature (T_{rec}) served as a stressor and immediately elicited SIH. Then, the foxes received either the anxiolytic drugs, diazepam or buspirone, or sterile saline. T_{rec} in the foxes treated with diazepam and buspirone was significantly lower 90min after treatment. The results indicate that SIH induced by handling was attenuated by anxiolytic drugs, which supports the hypothesis that anxiety contributes to the development of SIH.*

Keywords: *animal welfare, fear, silver fox, stress-induced hyperthermia*

Introduction

The silver fox (*Vulpes vulpes*) is a semi-domesticated dark mutation of the red fox that is farmed for fur production. Most silver foxes fear humans and this is recognized as a central problem in fox farming. Experiments in genetic selection of less fearful foxes were initiated in Russia in the late 1950s (Belyaev 1979). Pedersen (1994) found that early handling of silver fox cubs reduced their fear responses later in life. Current joint Nordic research initiatives include investigations into the effects of both early socialization and genetic selection for reduced fearfulness, as a means to improve the welfare of farmed fur-bearing animals. However, little is known about physiological variables related to fear or anxiety in silver foxes that could supplement behavioural studies.

Our recent studies indicated that silver foxes display stress-induced hyperthermia (SIH) immediately after the onset of handling and during physical restraint, as well as in the mere presence of man (Moe & Bakken 1997a,b). SIH in laboratory rodents is suppressed by treatment with anxiolytic drugs, suggesting an involvement of anxiety in the SIH response (Borsini *et al* 1989, 1993; Lecci *et al* 1990a,b).

The aim of the present study was to determine whether SIH represents a physiological indicator of fear or anxiety in farmed silver foxes. More specifically, we wanted to find out whether SIH induced by handling could be attenuated by pretreatment with the anxiolytic drugs diazepam or buspirone.

Materials and methods

In January 1996, 18 adult silver fox vixens were randomly divided into three groups: DIA (n = 6), BUS (n = 6) and CON (n = 6). Each vixen was housed individually in a traditional cage system for foxes in an outdoor fur shed. The foxes were not used to being handled.

Measuring T_{rec} served as the experimental stressor, since previous studies in foxes with surgically implanted radio-telemetry devices showed that i) handling elicits SIH within few minutes and within the time necessary to measure T_{rec}, and ii) T_{rec} was comparable with deep body temperature (T_b) in handled or physically restrained silver foxes (Moe & Bakken 1997b; Moe unpublished observations). A stockman with whom the animals were familiar lifted the animals out of their cage within approximately 15s using a neck tong for foxes. All animals were visually observed shortly before and during capture. T_{rec} was measured in all foxes using a standard, commercially available digital thermometer with an accuracy of $\pm 0.1^{\circ}C$ inserted 4cm into the rectum, and recorded after approximately 1min. Thereafter, the groups DIA, BUS and CON were injected intramuscularly with 5mg kg^{-1} diazepam (Vival® AL, Norway), 10mg kg^{-1} buspirone in 10ml sterile saline (Buspar®, Bristol-Myers, USA) or vehicle (sterile saline), respectively. The drug dosage was based on the results of studies in mice (Lecci *et al* 1990b) and preliminary experiments in four silver foxes. After 90min, T_{rec} was recorded according to the procedure described above.

Differences in T_{rec} between groups before and after treatment were analysed statistically with pairwise *t*-tests using General Linear Models (GLM) procedures in the SAS system (Statistical Analysis Systems Institute Inc 1986). Results are presented as group means $\pm$SEM.

Results

The initial T_{rec} did not differ between groups (CON: $39.4 \pm 0.2^{\circ}C$; DIA: $39.4 \pm 0.2^{\circ}C$; BUS: $39.7 \pm 0.2^{\circ}C$; ns). All foxes withdrew into a corner of the cage shortly before being caught, but did not show any other strong attempts to flee or markedly elevated levels of physical activity. After 90min, T_{rec} in CON was $39.4 \pm 0.2^{\circ}C$, whereas T_{rec} in DIA and BUS was $38.3 \pm 0.20^{\circ}C$ and $37.9 \pm 0.2^{\circ}C$ respectively, both differing significantly from CON ($P < 0.001$ and $P < 0.0001$, respectively). T_{rec} in DIA and BUS did not differ significantly between groups. Two of the foxes treated with diazepam showed mild sedation, but no sedation was observed in foxes treated with buspirone or vehicle at 90min post-treatment.

Discussion

The initial T_{rec} in all groups, and the T_{rec} of the controls 90min after treatment, were elevated when compared with basal T_b of 38.0-38.6°C measured with transmitter implants in other unhandled silver foxes (Moe & Bakken 1997a, b). However, T_{rec} in the present study was similar to previously observed T_{rec} and T_b during handling and physical restraint (Moe & Bakken 1997b). Thus, the foxes in the present study were considered to have evoked SIH within the time taken to measure T_{rec}, as also noted in these earlier studies.

The present study indicated that SIH induced by handling was prevented by pretreatment with anxiolytic drugs. Similarly, SIH induced by the fear of handling was antagonized by similar drugs in laboratory rodents (Borsini *et al* 1989, 1993; Lecci *et al* 1990a, b). Thus,

the results may indicate that SIH also involves fear or anxiety in silver foxes. The anxiolytic action of diazepam is mediated via benzo-diazepine receptors in the CNS and potentiates the inhibitory effect of gamma-aminobutyric acid (GABA), whereas buspirone activates 5-HT_{1A} receptors and induces a decrease in serotoninergic transmission (Mennini *et al* 1987). The temperature reduction after treatment with both drugs points to a possible relation between these systems and the mechanism of SIH in the silver fox.

Muscular relaxation due to diazepam (Mennini *et al* 1987), as indicated by mild sedation in two foxes, may have inhibited thermoregulation. However, muscle relaxants did not attenuate SIH in mice (Lecci *et al* 1990b). Furthermore, after treatment with buspirone no signs of sedation were observed, whereas SIH was apparently attenuated. This is in agreement with observations that buspirone does not exert any sedative or muscle relaxant effects (Mennini *et al* 1987), but attenuates SIH in mice (Lecci *et al* 1990b).

Our findings indicate that the serotoninergic system may be involved in the SIH response in silver foxes. Interestingly, Russian studies of silver foxes genetically selected for reduced fearfulness have suggested an involvement of serotoninergic pathways in fear responses in this species (Plyusnina *et al* 1991).

Emotional involvement in the origin of SIH was supported by the finding that the foxes withdrew from the handler, which indicates a behavioural fear response (Pedersen 1994). Our recent studies with surgically implanted radio-telemetry devices showed that the mere presence of a human elicited SIH in silver foxes (Moe & Bakken 1997a). Furthermore, SIH in the foxes withdrawing from humans was of a greater magnitude than in those remaining in the front of the cage, and the SIH response was gradually diminished by positive conditioned learning (Bakken *et al* 1993), which suggests anxiety or fear contribute to the SIH response in silver foxes. Since the foxes in the present study did not show any markedly elevated levels of physical activity, SIH cannot be solely ascribed to an increased heat load due to increased physical activity, as has been noted in laboratory rodents (Kluger *et al* 1987; Borsini *et al* 1989).

As the experimental foxes were not equipped with radio-telemetry devices, it was not possible to elucidate whether the decreased T_{rec} after treatment with anxiolytics was due to an impact of the drugs on the basal body temperature rather than on SIH. However, neither diazepam nor buspirone were found to lower the basal body temperature in mice (Lecci *et al* 1990b). Furthermore, T_{rec} in foxes treated with anxiolytics fell within the range of basal temperatures recorded for other undisturbed foxes measured with transmitters (Moe & Bakken 1997a,b).

Conclusion

The results of the present study indicate that anxiolytic drugs prevented SIH induced by handling in silver foxes and thus suggest an involvement of anxiety in the SIH response in this species. SIH, measured with surgically implanted transmitters, may therefore be a promising physiological indicator of anxiety or fear that can be applied as a means to supplement behavioural research when assessing fear responses in farmed foxes in studies concentrating on animal welfare. At present, this is one subject of our further research.

Animal welfare implications

Assessment of welfare is a necessary basis for any improvement in the welfare of farmed silver foxes. There is therefore an increasing need to be able to assess stress and fear responses not only by means of behavioural observations, but also by supplementing these studies with relevant physiological parameters. The present paper, and ongoing work, suggest that stress-induced hyperthermia (SIH) could be used as a possible measurement of fear or anxiety responses. Our further research will focus on the applicability of SIH measured with surgically implanted radio-telemetry devices for behavioural research and welfare studies in farmed silver foxes. We hope that this work will contribute to increased welfare in this species.

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