

Provided for non-commercial research and education use.
Not for reproduction, distribution or commercial use.



This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

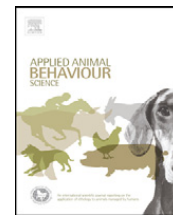
In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

<http://www.elsevier.com/copyright>



Contents lists available at ScienceDirect

Applied Animal Behaviour Science

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

The influence of handling and exposure to a ferret on body temperature and running wheel activity of golden hamsters (*Mesocricetus auratus*)

Patrizia Eberli, Sabine G. Gebhardt-Henrich*, Andreas Steiger

Division of Animal Housing and Welfare, Vetsuisse Faculty, P.O. Box, CH-3001 Berne, Switzerland

ARTICLE INFO

Article history:

Accepted 21 February 2011

Keywords:

Golden hamster
Stress
Ferret
Handling
Running wheel
Emotional fever

ABSTRACT

In order to determine a stress response, two groups of twenty male golden hamsters were either exposed to a ferret or handled by a human. The hamsters' body temperature and running wheel activity were measured as stress correlates. Half of the hamsters' cages were equipped with a functional running wheel to determine whether the presence of a running wheel might reduce stress. Exposure to the ferret was followed by a significant increase in body temperature and running wheel revolutions; however, running wheel activity did not change after handling. Body temperature increased less after handling in hamsters living in a cage with a functional running wheel than in those with a non-revolving running wheel. This suggests that hamsters with a functional running wheel reacted less strongly to acute stress caused by handling. On the other hand, temperature increase after the exposure to a ferret was not affected by the presence of a running wheel. Both exposure to a ferret and handling caused stress in golden hamsters, as demonstrated by an increase in body temperature (emotional fever). Stress caused by handling was much milder than stress caused by the ferret.

© 2011 Elsevier B.V. All rights reserved.

1. Introduction

Exposure to potential predators represents one of the most severe stressors as survival is at stake (Blanchard et al., 1989). In households with golden hamsters, there are often other pets such as cats and dogs, less often also ferrets. So the question arises if the presence of potential predators causes stress in golden hamsters. The present study dealt with the effects of two stressors, the presence of a ferret as a natural predator and handling by humans, on golden hamsters. Handling occurs more or less frequently in both pet and laboratory hamsters. We ana-

lyzed how hamsters that had not been handled by humans after weaning responded to handling. Predator presence, predator odours and handling can cause stress in rodents (Adamec and Shallow, 1993; Adamec et al., 2004; Belzung et al., 2001; Blanchard et al., 1998; Dielenberg et al., 2001; Gattermann and Weinandy, 1996/97; Masini et al., 2005). We chose a ferret as a predator of hamsters because they are known to elicit a distinctive stress response in rats (Masini et al., 2005) and their popularity as a pet is growing. Closely related species of the undomesticated ancestor of the ferret (*Mustela* sp.) used to occur all over Eurasia. Using natural predators can avoid some artefacts when studying anxiety (Staples, 2010). However, natural predators have gone extinct in the range of golden hamsters (Gattermann, pers. comm.). In evolutionary terms, ferrets closely resemble a natural predator. The prediction was that a ferret would elicit a very strong stress response.

Since stress decreases animal welfare, we examined and validated two possibilities of detecting and measur-

* Corresponding author. Present address: Centre of Proper Housing of Poultry and Rabbits (ZTHZ), Burgerweg 22, CH-3052 Zollikofen, Switzerland. Tel.: +41 31 915 3513; fax: +41 31 915 3514.

E-mail address: sabine.gebhardt@bvet.admin.ch (S.G. Gebhardt-Henrich).

ing acute stress in golden hamsters. We measured the golden hamsters' body temperatures and their running wheel activity before and after the potentially stressful situation of exposure to a ferret or handling.

So far, detecting and measuring stress using stress hormones such as cortisol in the blood and feces of golden hamsters has yielded unsatisfactory results (Gebhardt-Henrich et al., 2007; but see Chelini et al., 2010). We used body temperature instead, measured telemetrically in order to detect emotional fever. Emotional fever is a true fever and not only hyperthermia (Briese and Cabanac, 1991; Kluger et al., 1987) and occurs in all mammals, birds and reptiles (Cabanac, 1999). In contrast to hyperthermia, which can result from increased metabolic activity and is defined as an increase in central temperature above the set-point, fever is regulated by the central nervous system which raises the set-point to a higher level and therefore adjusts the body temperature.

Additionally, we recorded the number of running wheel revolutions and behaviour in order to detect further effects of acute stress in the animals. The presence of a running wheel could influence stress severity. It is known that physical exercise can reduce stress (Adlard and Cotman, 2004; Greenwood et al., 2005; Moraska and Fleshner, 2001). Our second goal was therefore to investigate whether golden hamsters living in a cage equipped with a functional running wheel displayed fewer stress symptoms than those living in a cage with a non-functional running wheel.

The study's objective was to demonstrate the effect of handling and the effect of a ferret as stressors and to test whether the stressors affected body temperature and behaviour.

2. Animals, materials, and methods

2.1. Animals and housing conditions

Forty male golden hamsters from 17 litters (progeny of the strain Rj: AURA (SPF Han), Elevage Janvier, Le Genest Saint Isle; genealogy of parents was unknown) were weaned between days 28 and 32.

The hamsters were placed singly into commercially available wire cages with plastic bottoms (length \times width \times height: 97 cm \times 57 cm \times 45 cm).

The cages were equipped with a running wheel, which had a diameter of 30 cm and a running surface consisting of a perforated metal plate (width: 10 cm) with holes (\varnothing 5 mm) to prevent leg injuries (Mrosovsky et al., 1998). One revolution of the running wheel corresponds to 94.25 cm. Half of the wheels were fixed and did not turn. They are called 'non-functional' wheels hereafter.

Wood shavings (Allspan[®]) to a depth of approximately 10 cm and a handful of hay were used as bedding. Further structures offered to the animals were a wooden bottomless shelter (length \times width \times height: 20 cm \times 14 cm \times 14 cm) with an entrance hole of 5 cm in diameter on the side of the box, a cardboard tube (\varnothing 4 cm, length 10 cm), a hazel branch, a bowl filled with fine sand (\varnothing 16 cm), paper towels as nesting material, a feeding bowl, and a water bottle.

An artificial 12 h dark–12 h light cycle was maintained, darkness began at 14:00 h (CEST).

Grain feed (Schweizer[®]) was offered ad libitum, and additionally fresh fruits and vegetables (apple, carrot, chicory, and fennel) were provided daily. Low fat curd cheese was provided once a week as a protein source. Water was available ad libitum in bottles.

Cages were cleaned every two weeks by replacing the soiled portions of bedding. From the beginning of the experiment during the cage cleaning procedure, special precautions were taken to make sure that the hamsters that were in the handling experiment did not get used to the handling procedure. They were never taken out of their cage by hand, but with the help of a tube made of red transparent acrylic glass. They entered this tube voluntarily and could therefore be taken out of the cage easily. During the implantation of the transponder these hamsters were handled while being anaesthetized.

All hamsters were kept in a room with a temperature between 18 °C and 22 °C during the experiments. The humidity was unregulated.

2.2. Experiments

The project consisted of two experiments: the first experiment subjected the animals to a ferret and the second to human handling. Each hamster was subjected to the experimental treatment (handling or ferret) at one time and also served as its own control. Hamsters exposed to ferrets were not handled, i.e. each hamster was only subjected once to a stressor. The design and abbreviations are shown in Table 1.

2.2.1. Ferret exposure

Twenty hamsters were assigned randomly to either a group with a functional running wheel or to one with a non-functional running wheel; each group consisted of ten hamsters (Table 1).

Each hamster was exposed once and served as a control once (control means: only measuring body temperature, registering running wheel activity and recording its behaviour, no ferret exposure).

On one day, one FE-fRW and one FE-nfRW were exposed and one FC-fRW and one FC-nfRW were used as controls.

During the 10 min of exposure to a female ferret, the hamster was in a wire cage, which was placed inside the ferret's cage (length \times width \times height: 110 cm \times 69 cm \times 180 cm). There was no shelter in the hamster's cage, so the hamster could see, smell and hear the ferret during the whole duration of exposure. On the lower 15 cm of the cage, the wire bars were wrapped with plastic to ensure that the ferret could not bite the hamster through the wire.

To minimise carry over effects, there was a minimal time lag for each hamster of three weeks between the control and the exposure (Adamec and Shallow, 1993). The treatments were carried out when the hamsters were between 3.5 and 4.5 months old.

Table 1

Experimental design with sample sizes and abbreviations which are used throughout the paper.

Experiment	Ferret				Handling			
	Functional		Non-functional		Functional		Non-functional	
Running wheel	fRW		nfRW		fRW		nfRW	
Abbreviation	fRW		nfRW		fRW		nfRW	
Treatment	Yes	Control	Yes	Control	Yes	Control	Yes	Control
Abbreviation	FE	FC	FE	FC	HE	HC	HE	HC
N	10		10		10		10	

2.2.2. Handling

Another batch of twenty hamsters was assigned randomly to a group with a functional or to a group with a non-functional running wheel. Each hamster was handled once and served as a control once (control means: only measuring body temperature, registering running wheel activity and recording its behaviour, no handling).

Hamsters were handled for 10 min, following a previously defined protocol which consisted of holding them tightly in the hand (twice for 2 min), manual fixation including turning the hamsters on their backs (2 min), releasing the hamsters and catching them again (5 times in 2 min), and petting (2 min). The same person (P.E.) always handled the hamsters and she was also present in the rooms at other times feeding and cleaning the cages. There was a minimal time lag for each hamster of three weeks between the control and handling. The treatments were carried out when the hamsters were between 6 and 7 months old.

2.3. Measurements

2.3.1. Body temperature

Body temperature was measured telemetrically using the transponders IPTT-200 and the wireless reader system WAS-5001 by PLEXX (Elst, The Netherlands). A transponder was subcutaneously implanted during a short (1 min) isofluran anaesthesia at least three weeks before the experiments. Isofluran was led into a small chamber and the hamster was put into the chamber until it became unconscious. Using telemetry to measure body temperature minimised the possibility that measuring the temperature itself could be a source of stress (Clark et al., 2003). However, the shelter was lifted and the distance of the reader to the hamster was a few centimetres. Most sleeping hamsters woke up when their body temperature was taken.

Body temperature was measured immediately before and after the ferret exposure or the handling treatment. This was always done at the same time of the day at the end of the dark period. The body temperature of a control hamster was measured simultaneously.

2.3.2. Running wheel activity and general behaviour

The running wheel activity (only possible in functional wheels) was continuously registered using The Chronobiology Kit[®] (Stanford System). Revolutions 24 h before stressor application and 24 h after stressor application were counted and compared. The same was done for control hamsters. Animals were video-taped twice for 3 h after stressor application or at the same time for control hamsters (session 1: 16:00–19:00 h, session 2: 20:00–23:00 h).

Session 1 covers the time of highest activity of the hamsters (unpublished data). They were videotaped in the dark, using infrared sensitive cameras (Ikegami ICD-47E) and their behaviour was recorded on video (Panasonic AG-6730). The overall activity time for each hamster was determined. A hamster was considered as being active as soon as it could be seen on the recording, which means that it was not hidden in its shelter. The total activity time was divided into six intervals. The hamster's behaviour in the first 5 min of each interval was analyzed using The Observer[®] Version 5.1. Thus, there was a total of 30 min that were behaviourally analyzed in each recording session. Whenever a hamster was inactive for an entire hour, the 5 min of activity closest to the planned hour were analyzed.

Behaviours were recorded using the system by Hauzenberger et al. (2006) and included locomotion, body positions and the location in the cage.

2.3.3. Body weight and weight of adrenal glands

Four days after the end of the experiments, when the hamsters were between 22 and 30 weeks of age, they were euthanized, using a combination of medetomidine (Domitor[®]), ketamine (Ketasol[®]) and pentobarbital (Vetanarcol[®]).

Body weight was determined and the adrenal glands were removed, trimmed of excess fat and connective tissue and weighed. To obtain the parameter 'averaged weight' the weights of the right and left adrenal glands of each hamster were added and divided by two. To adjust the weights of the adrenal glands to the body weights of the hamsters, the residuals of the linear regression of the weight of the averaged adrenal glands on body weight were used.

2.4. Statistics

Statistical analyses were carried out using NCSS 2004[®] and SAS 9.1[®] statistical software packages. Data and residuals were checked for normality with these software packages. Analyses with one value per hamster were analyzed by general linear models (Proc GLM, SAS 9.1[®]). Analyses using two observations per animal were analyzed by mixed general linear models for repeated measures using the individual as the (random) subject variable (Proc Mixed, SAS 9.1[®]). Full models using all interactions were calculated and afterwards clearly non-significant interactions ($P > 0.2$) were pooled. Treatment effects on running wheel revolutions were estimated as the difference between the measurements 24 h before and after the treatment. A non-parametric sign test was used where the number of observations below and above the mean was analyzed. All correlation coefficients are Pearson's. The

Table 2

Baseline body temperatures [$^{\circ}\text{C}$ (\pm standard deviation)] of hamsters, measured before the experimental treatment or before serving as a control. The *P*-values refer to a GLM-ANOVA. The Bonferroni adjustment for multiple tests was used by dividing 0.05 by the number of tests per column. The significant value is denoted by an asterisk.

All hamsters	36.22 \pm 0.54	<i>P</i> =0.15	Predator exposure	35.78 \pm 0.19	<i>P</i> =0.40	FE	35.71 \pm 0.20	<i>P</i> =0.27
				35.92 \pm 0.68		FC	35.99 \pm 0.75	
	36.02 \pm 0.65		Handling	36.65 \pm 0.41	<i>P</i> =0.003*	HE	36.68 \pm 0.41	<i>P</i> =0.024
				36.13 \pm 0.62		HC	36.62 \pm 0.42	
							36.21 \pm 0.52	

Shaded part denotes functional running wheel.
 Non-shaded part denotes non-functional running wheel.

experiments were approved by the Bernese Cantonal Office of Agriculture and Nature according to the Swiss Animal Protection Legislation including animal ethics.

3. Results

3.1. Body temperature

The average baseline body temperature of the hamsters in both experiments (measured before the experimental treatment, respectively at the same time in control hamsters) was $36.12 \pm 0.60^{\circ}\text{C}$, range $34.8\text{--}37.6^{\circ}\text{C}$). Baseline body temperatures are given in Table 2. The presence of a fRW had no influence on baseline body temperature measured before the experiment in the ferret exposure experiment (abbreviations see Table 1).

In contrast, there were significant differences in baseline body temperature between hamsters with fRW or nFRW in the handling experiment. The baseline body temperature of hamsters with fRW was significantly higher than the baseline body temperature of hamsters with a nFRW (Table 2).

Comparing baseline body temperatures of all hamsters in both experiments, no significant differences were found, although hamsters with a fRW tended to have a higher body temperature than those with a nFRW.

3.1.1. Ferret exposure experiment

The average body temperature of ferret exposed hamsters increased by 2.36°C ($\pm 0.77^{\circ}\text{C}$, range $0.7\text{--}3.5^{\circ}\text{C}$), while the body temperature of control hamsters rose by 0.69°C on average ($\pm 0.82^{\circ}\text{C}$, range $0.4\text{--}2.3^{\circ}\text{C}$). This difference in temperature increase was highly significant (repeated measures: $P < 0.0001$, $F_{1,18} = 44.22$, $N = 20$), but was not affected by the presence of a functional running wheel. Changes in body temperature are illustrated in Fig. 1.

3.1.2. Handling

The average increase in body temperature of handled hamsters was 0.94°C ($\pm 0.68^{\circ}\text{C}$, range $0.2\text{--}2.3^{\circ}\text{C}$), while body temperature of control hamsters rose 0.26°C on average ($\pm 0.47^{\circ}\text{C}$, range $0.9\text{--}1.0^{\circ}\text{C}$). This difference in the increase of the body temperature was highly significant and there was also a significant influence of the presence of a running wheel (repeated measures: running wheel: $P = 0.05$, $F_{1,18} = 4.43$, handling: $P = 0.0007$, $F_{1,18} = 16.5$, inter-

action: $P = 0.03$, $F_{1,18} = 5.77$, $N = 20$). The increase in body temperature due to handling was significantly higher in hamsters with a nFRW ($1.32^{\circ}\text{C} \pm 0.59$) than with a fRW ($0.56^{\circ}\text{C} \pm 0.56$). In control hamsters, there was no significant difference in the increase of the body temperature between animals with a fRW and with a nFRW. Changes in body temperature are illustrated in Fig. 1.

The increase in body temperature differed between hamsters exposed to the ferret and those exposed to handling (repeated measures: $P = 0.003$, $F_{1,36} = 10.6$, $N = 40$) (Fig. 1). Additionally, the functioning of the running wheel affected both groups differently as shown by the significant three-way interaction between wheel, control/treatment, ferret/handling (same analysis: $P = 0.02$, $F_{1,36} = 6.07$, $N = 40$).

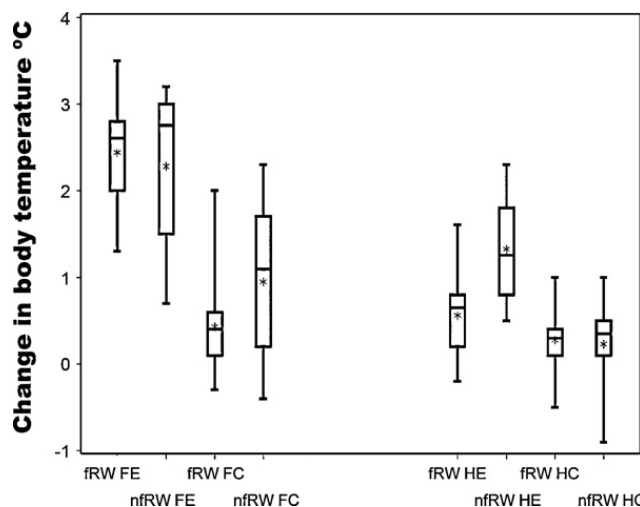


Fig. 1. Change in body temperature in the ferret exposure and handling experiments (difference between the body temperature after ferret exposure/handling or control and the body temperature before ferret exposure/handling or control). The horizontal line is the median, the box encloses the interquartile range of the data. The upper and lower T-lines show the range. The following abbreviations are used in the figure—fRW FE: ferret exposure experiment for hamsters with a functional running wheel at the time of exposure, nFRW FE: the same for hamsters without functional running wheels, fRW FC: ferret exposure experiment for hamsters with a functional running wheel at the time of control measurements, nFRW FC: the same for hamsters without functional running wheels, fRW HE: handling experiment for hamsters with a functional running wheel at the time of exposure, nFRW HE: the same for hamsters without functional running wheels, fRW HC: handling experiment for hamsters with a functional running wheel at the time of control measurements, and nFRW HC: the same for hamsters without functional running wheels.

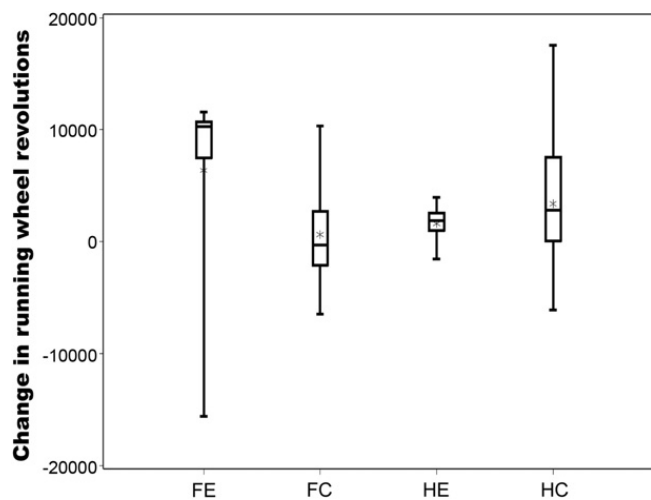


Fig. 2. Change in running wheel revolutions in the ferret exposure and handling experiments (difference between day of ferret exposure/handling or control and day before ferret exposure/handling or control). The following abbreviations are used in the figure—FE: ferret exposure experiment at the time of exposure, FC: same experiment but at the time of control measurements, HE: handling experiment after handling, HC: handling experiment at the time of control measurements.

3.2. Running wheel activity and general behaviour

All fRW hamsters used their running wheel. The average distance (calculated by using the number of revolutions) in the 24 h before the experimental treatment (either after exposure/handling or measurement of body temperature as a matched control) was 13.17 km (13,959 revolutions) with a minimum of 57 m (60 revolutions) and a maximum of 21.04 km (22,319 revolutions).

3.2.1. Ferret exposure

In the night before the experimental treatment, the hamsters performed an average number of 14,426 (± 2006) running wheel revolutions. After exposure to the ferret, they increased their running wheel activity by an average of 6360 (± 2873) additional revolutions (a total of $20,786 \pm 3093$ revolutions, minimum 2317, maximum 29,546). The numbers of running wheel revolutions on the day before the experimental treatment and the day of the experimental treatment were significantly different ($P < 0.04$, sign test $M = 3.5$, $N = 9$). Control hamsters performed an average number of 16,438 (± 1566) running wheel revolutions. After the control measurements, they increased their running wheel activity by an average of 632 (± 1580) additional revolutions (a total of $17,070 \pm 2217$ revolutions, range 3920–25,512) (Fig. 2). The numbers of running wheel revolutions on the day before the experimental treatment and the day of the experimental treatment were not significantly different ($P = 1$, sign test $M = -0.5$, $N = 9$) for the control hamsters.

3.2.2. Handling

In the night before the experimental treatment, the hamsters performed an average number of 13,768 (± 6684) running wheel revolutions. After handling, they increased their number of revolutions by an average of 1609 (± 1762 , range 1549–3965) additional turns compared

with the preceding day ($15,377 \pm 5375$ revolutions, range 4226–21,408). The numbers of running wheel revolutions on the day before the experimental treatment and the day of the experimental treatment were not significantly different (NS, $M = 2.5$, $N = 9$) for the handled hamsters.

Numbers of running wheel revolutions of control hamsters did not differ significantly between control day and the day before. The difference in the number of running wheel revolutions between the experimentally treated hamsters and their control values tended to be higher in ferret exposed hamsters (general linear model: $P = 0.057$, $F_{1,16} = 4.19$, $N = 17$) than in handled hamsters.

Besides running wheel activity other elements of behaviour were not affected by the treatments.

3.2.3. Correlation between running wheel activity and body temperature

Increases in body temperature and in running wheel activity tended to be correlated in the ferret exposure experiment ($r_p = 0.59$, $P < 0.1$, $N = 9$), but not in the handling experiment ($r_p = -0.03$, $P = 0.95$, $N = 9$).

3.3. Body weight, and weight of adrenal glands

3.3.1. Body weight

Hamsters of the ferret exposure experiment had a mean body weight of 103.7 g (± 10.4 g, range 87.3–133.4 g) at the time of euthanasia (age = 21–22 weeks).

Hamsters of the handling experiment had a mean body weight of 118.2 g (± 7.4 g, range 101.5–132.1 g) at the time of euthanasia (age = 28–29 weeks). There were no significant differences between the body weights of the hamsters with fRW or nRW, neither in the ferret experiment nor in the handling experiment (GLM: ferret: $F_{1,18} = 0.89$, $P = 0.36$, handling: $F_{1,18} = 1.3$, $P = 0.27$).

3.3.2. Weight of adrenal glands

Unaveraged weights of the right and left adrenal glands were correlated within individual ($r_p = 0.43$, $P < 0.007$, $N = 39$). Hamsters of the handling experiment had bigger adrenal glands and those living in a cage equipped with fRW tended to have bigger adrenal glands (general linear model of the averaged weights: type of experiment: $P = 0.0002$, $F_{1,36} = 16.76$, wheel: $P = 0.07$, $F_{1,36} = 3.55$, $N = 39$) than hamsters with nRW (Table 3). When body weight was taken into account by using the residuals of the adrenals they were significantly larger in hamsters living in a cage equipped with a fRW and they tended to be larger in the handling experiment (general linear model: wheel: $F_{1,36} = 6.55$, $P = 0.015$, type of experiment: $F_{1,36} = 3.03$, $P = 0.09$, $N = 39$, Table 3).

4. Discussion

The largest increase in body temperature was found in the hamsters that had been exposed to a ferret. Assuming that exposure to a ferret is a stressful situation, this demonstrates that stress in hamsters can be detected by measuring their body temperature. Some hamsters were woken up by taking their temperature. The small increase in the body temperature of the control animals could be

Table 3

Averaged weights and residuals $\times 10^{-4}$ [g] of adrenal glands and their percentage of the total body weight of hamsters of the exposure and the handling experiments with and without functional running wheels. A regression of the averaged weights of the adrenal glands on body weight yielded the residuals. Standard errors are given.

	Exposure		Handling	
	Wheel	No wheel	Wheel	No wheel
Average	114.95 \pm 6.44	108.5 \pm 4.8	144.25 \pm 5.76	127.89 \pm 6.98
Percentage	1.13 \pm 0.05	1.04 \pm 0.06	1.23 \pm 0.04	1.07 \pm 0.05
Residual	0.67 \pm 10.70	-20.93 \pm 12.68	28.52 \pm 10.28	-9.17 \pm 12.58
N	10	10	10	9

explained by the increased activity during wake-up or by assuming that even measuring the temperature telemetrically caused a certain degree of stress in some animals. The increase in body temperature of handled hamsters shows that handling also is a stressful event for golden hamsters. However, temperature increases were more pronounced in hamsters exposed to the ferret than in handled hamsters. This indicates that stress caused by handling is less severe than stress caused by the presence of a ferret. This result is consistent with the findings by Gattermann and Weinandy (1996/97). The reason for the difference could be that all hamsters were habituated to the smell and presence of humans but had never smelled a ferret before the treatment. It is not clear, how hamsters with early exposure to the smell of ferrets would react to these animals. Normally, hamsters are handled more frequently than in our handling experiment. Therefore, the stress response due to handling could be even weaker if hamsters had been habituated to humans by frequent handling.

In humans it was shown that regular exercise has numerous, mostly positive consequences. Chaouloff (1989) demonstrated that there was a close link between exercise and mental health in humans. Dishman (1997) confirmed such effects in other animals. Physical activity reduces symptoms of depression and fear and improves the well-being and the reactions to stress. Therefore the question arises whether such a positive effect can also be demonstrated in golden hamsters subjected to stressors. Running regularly in a running wheel or on a treadmill could have an antidepressive and anxiolytic effect.

Our results are difficult to interpret in this context. Body temperature of handled hamsters with a wheel increased less than in control hamsters without a functional wheel, but this was not true for the hamsters exposed to the ferret. A possible reason could be that our handled hamsters were a few weeks older than the ferret exposed hamsters which had had longer exposure to fRW or nRW. Another explanation is that exposure to a ferret caused such severe stress that the running wheel had no alleviating effect, while handling was just moderately stressful and a fRW enabled the hamsters to cope. The smaller increase might also result from the significantly higher baseline body temperature when living in a cage equipped with a fRW, as described by Golombek et al. (1993).

Using a running wheel is much easier than running on the ground meaning that the distance covered by running in the wheel is not the same distance as the animals would have covered on the ground under natural conditions. When a golden hamster moves in the open field, it has

to cope with various soil conditions, or inclined and sloping ground, which is linked with additional effort (Vonlanthen, 2003).

The reason for the increase in running wheel activity could be that under natural conditions a place with a ferret is no longer safe. Running in the wheel might give the hamster the illusion of leaving the dangerous place. This possibility is consistent with the theory that running wheel activity is linked to explorative and flight behaviour (Mather, 1981). Alternatively, running in the wheel could have represented displacement behaviour.

Like body temperature, the number of running wheel revolutions increased more after exposure to a ferret than after handling. If it is assumed that the increase in running wheel activity is proportional to the increase in stress, these results could be another confirmation for the hypothesis that the presence of a ferret causes more severe stress than handling. Running in a wheel might increase body temperature by itself due to increased activity. However, the increase in body temperature was measured before the hamsters were running in the wheel. To our knowledge, no studies have yet linked an increase in running wheel activity to stress. The correlation, although non-significant, between the increase in body temperature and the increase in running wheel activity in the ferret exposure experiment might suggest such a link. This might only hold for severely stressful situations, because the running wheel activity only significantly increased in the ferret exposure experiment but not in the handling experiment. Therefore the increase in body temperature might be a more sensitive tool to measure stress than the increase in running wheel revolutions. General behaviour was not useful for the detection of stress in this experiment.

For technical reasons the ages of the hamsters in the ferret exposure and the handling experiment differed. Running wheel activity decreases with progressing age (Sherwin, 1998; Vonlanthen, 2003; Gebhardt-Henrich et al., 2005). However, baseline running wheel activity did not differ significantly between ferret exposed and handled hamsters, so the two groups can be compared. In both experiments animals were still young adults, which use the running wheel most of all (Vonlanthen, 2003).

The presence of a functional wheel was associated with significantly greater adrenal glands when adjusted for body weight. Absolute values of the weights of adrenal glands did just not differ significantly. Heavier adrenal glands could be related to chronic stress. Since measuring the weight of the adrenal glands has a substantial margin of error, it would be interesting to do histological examinations in a further

study in order to examine whether there is chronic stress due to the presence of a fRW.

5. Conclusions

Both the presence of a ferret and handling by a human caused stress in golden hamsters. Therefore, owners of golden hamsters should not keep ferrets in the same room as the hamster. The stress caused by handling was not as severe as exposure to the ferret. Therefore, moderate handling, e.g. by the owner, the veterinarian or the lab technician might not cause excessive stress.

The results of the body temperature suggested that hamsters living in a cage with a functional running wheel reacted less severely to moderate stress caused by handling than if the running wheel was non-functional. Therefore an appropriate running wheel should be made available.

Acknowledgements

We thank Jean Michel Hatt for letting us lend two ferrets. P.E. received a doctoral grant of the Federal Veterinary Office. Andrina Hauzenberger, Silvan Urfer, Evi Waiblinger and two anonymous reviewers commented on the manuscript and greatly improved it.

References

- Adamec, R.E., Shallow, T., 1993. Lasting effects on rodent anxiety of a single exposure to a cat. *Physiol. Behav.* 54, 101–109.
- Adamec, R., Walling, S., Burton, P., 2004. Long-lasting, selective, anxiogenic effects of feline predator stress in mice. *Physiol. Behav.* 83, 401–410.
- Adlard, P.A., Cotman, C.W., 2004. Voluntary exercise protects against stress-induced decreases in brain-derived neurotrophic factor protein expression. *Neuroscience* 124, 985–992.
- Belzung, C., El Hage, W., Moindrot, N., Griebel, G., 2001. Behavioral and neurochemical changes following predatory stress in mice. *Neuropharmacology* 41, 400–408.
- Blanchard, R.J., Blanchard, D.C., Hori, K., 1989. An ethoexperimental approach to the study of defense. In: *Ethoexperimental Approaches to the Study of Behavior*. Kluwer, Dordrecht, pp. 114–136.
- Blanchard, R.J., Nikulina, J.N., Sakai, R.R., McKittrick, C., McEwen, B., Blanchard, D.C., 1998. Behavioral and endocrine change following chronic predatory stress. *Physiol. Behav.* 63, 561–569.
- Briese, E., Cabanac, M., 1991. Stress hyperthermia: physiological arguments that it is a fever. *Physiol. Behav.* 49, 1153–1157.
- Cabanac, M., 1999. Emotion and phylogeny. *Jpn. J. Physiol.* 49, 1–10.
- Chaouloff, F., 1989. Physical exercise and brain monoamines: a review. *Acta Physiol. Scand.* 137, 1–13.
- Chelini, M.-O., Otta, E., Yamakita, C., Palme, R., 2010. Sex differences in the excretion of fecal glucocorticoid metabolites in the Syrian hamster. *J. Comp. Physiol. B: Biochem., Syst., Environ. Physiol.* 180, 919–925.
- Clark, D.L., DeBow, S.B., Iseke, M.D., Colbourne, F., 2003. Stress-induced fever after postischemic rectal temperature measurements in the gerbil. *Can. J. Physiol. Pharmacol.* 81, 880–883.
- Dielenberg, R.A., Carrive, P., McGregor, I.S., 2001. The cardiovascular and behavioral response to cat odor in rats: unconditioned and conditioned effects. *Brain Res.* 897, 228–237.
- Dishman, R.K., 1997. Brain monoamines, exercise, and behavioral stress: animal models. *Med. Sci. Sports Exerc.* 29, 63–74.
- Gattermann, R., Weinandy, R., 1996/97. Time of day and stress response to different stressors in experimental animals. Part I. Golden hamster (*Mesocricetus auratus* Waterhouse 1839). *J. Exp. Anim. Sci.* 38, 66–76.
- Gebhardt-Henrich, S.G., Vonlanthen, E.M., Steiger, A., 2005. How does the running wheel affect the behaviour and reproduction of golden hamsters kept as pets? *Appl. Anim. Behav. Sci.* 95, 199–203.
- Gebhardt-Henrich, S.G., Fischer, K., Hauzenberger, A.R., Keller, P., Steiger, A., 2007. The duration of capture and restraint during anesthesia and euthanasia influences glucocorticoid levels in male golden hamsters. *Lab Anim. (NY)* 36, 41–46.
- Greenwood, B.N., Foley, T.E., Burhans, D., Maier, S.F., Fleshner, M., 2005. The consequences of uncontrollable stress are sensitive to duration of prior wheel running. *Brain Res.* 1033, 164–178.
- Golombek, D.A., Ortega, G., Cardinali, D.P., 1993. Wheel running raises body temperature and changes the daily cycle in golden hamsters. *Physiol. Behav.* 53, 1049–1054.
- Hauzenberger, A., Gebhardt-Henrich, S.G., Steiger, A., 2006. The influence of bedding depth on behaviour in golden hamsters (*Mesocricetus auratus*). *Appl. Anim. Behav. Sci.* 100, 280–294.
- Kluger, M.J., O'Reilly, B., Shope, T.R., Vander, A.J., 1987. Further evidence that stress hyperthermia is a fever. *Physiol. Behav.* 39, 763–766.
- Masini, C.V., Sauer, S., Campeau, S., 2005. Ferret odor as a processive stress model in rats: neurochemical, behavioral, and endocrine evidence. *Behav. Neurosci.* 119, 280–292.
- Mather, J.G., 1981. Wheel-running activity: a new interpretation. *Mammal Rev.* 11, 41–51.
- Moraska, A., Fleshner, M., 2001. Voluntary physical activity prevents stress-induced behavioral depression and anti-KLH antibody suppression. *Am. J. Physiol. Regulatory Integrative Comp. Physiol.* 281, R484–R489.
- Mrosovsky, N., Salmon, P.A., Vrang, N., 1998. Revolutionary science: an improved running wheel for hamsters. *Chronobiol. Int.* 15, 147–158.
- Sherwin, C.M., 1998. The use and perceived importance of three resources which provide caged laboratory mice the opportunity for extended locomotion. *Appl. Anim. Behav. Sci.* 55, 353–367.
- Staples, L.G., 2010. Predator odor avoidance as a rodent model of anxiety: learning-mediated consequences beyond the initial exposure. *Neurobiol. Learn. Mem.* 94, 435–445.
- Vonlanthen, E.M., 2003. Einflüsse der Laufradnutzung auf ausgewählte ethologische, morphologische und reproduktionsbiologische Parameter beim Syrischen Goldhamster (*Mesocricetus auratus*). Dissertation Vetsuisse Faculty, University of Bern, Switzerland. www.ths.vetsuisse.unibe.ch.