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Coping styles in animals: current status in behavior and stress-physiology

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Abstract

This paper summarizes the current views on coping styles as a useful concept in understanding individual adaptive capacity and vulnerability to stress-related disease. Studies in feral populations indicate the existence of a proactive and a reactive coping style. These coping styles seem to play a role in the population ecology of the species. Despite domestication, genetic selection and inbreeding, the same coping styles can, to some extent, also be observed in laboratory and farm animals. Coping styles are characterized by consistent behavioral and neuroendocrine characteristics, some of which seem to be causally linked to each other. Evidence is accumulating that the two coping styles might explain a differential vulnerability to stress mediated disease due to the differential adaptive value of the two coping styles and the accompanying neuroendocrine differentiation. © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Psychosocial factors have long been recognized as important in health and disease both in man and in animals. It is not the physical characteristics of a certain aversive stimulus but rather the cognitive appraisal of that stimulus, which determines its aversive character and whether a state commonly described as stress is induced. The impact of aversive stimuli or stressors is determined by the ability of the organism to cope with the situation [1,2]. Several definitions of coping can be given [3]. In the present paper, we prefer to use the term coping as the behavioral and physiological efforts to master the situation [3,4]. Successful coping depends highly on the controllability and predictability of the stressor [5,6]. A consistent finding across species is that whenever environmental stressors are too demanding and the individual cannot cope, its health is in danger. For this reason, it is important to understand the mechanisms and factors underlying the individual's capacity to cope with environmental challenges. A wide variety of medical, psychological and animal studies demonstrate that individuals may differ in their coping capacities. Factors that have been shown to affect the individual's

coping capacity include genotype, development, early experience, social support, etc. Since many studies in humans indicate that coping mechanisms are important in health and disease [7], researchers have tried for a long time to determine the individual vulnerability to stress-related diseases using estimates of the individual coping capacity. One approach concerns attempts to classify coping responses into distinct coping styles. A coping style can be defined as a coherent set of behavioral and physiological stress responses which is consistent over time and which is characteristic to a certain group of individuals. It seems that coping styles have been shaped by evolution and form general adaptive response patterns in reaction to everyday challenges in the natural habitat. The concept of coping styles has been used in a wide variety of animal species (see Table 1). Despite the widespread use of the concept, it is not without debate [8]. This is due to several flaws in the studies using the concept. First, not all studies fulfill the criterion of coping style as a coherent set of behavioral and physiological characteristics because only one parameter has been studied. Second, the extent to which clearly distinct coping styles can be distinguished has been questioned [8,9]. Special attention will be given here to the frequency distribution of coping styles in a population, the consistency over time and the one-dimensional character of the concept of coping styles. Finally, one may wonder to

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Table 1

Overview of the species in which a strong individual differentiation has been observed that may reflect coping styles. The plus signs give a rough indication of the number of parameters on which the individual differentiation is based, i.e. + indicates a single parameter study, ++ indicates a multi-parameter study

Species	Behavioral parameters	Physiological parameters	Reference
Mouse (<i>Mus musculus domesticus</i>)	+ +	+ +	[13]
Rat (<i>Rattus norvegicus</i>)	+ +	+ +	[77]
Pig (<i>Sus scrofa</i>)	+ +	+ +	[20,37]
Tree shrew (<i>Tupaia belangeri</i>)	+ +	+ +	[78]
Cattle (<i>Bos taurus</i>)	+	+ +	[23]
Great tit (<i>Parus major</i>)	+ +		[19]
Chicken (<i>Gallus domesticus</i>)	+	+ +	[79]
Beech marten (<i>Martes foina</i>)	+		[80]
Stickleback (<i>Gasterosteus aculeatus</i>)	+ +		[24]
Rainbow trout (<i>Oncorhynchus mykiss</i>)	+	+	[81]
Rhesus monkey (<i>Macaca mulatta</i>)	+ +	+ +	[82]
Human (<i>Homo sapiens</i>)	+ +	+ +	[26]
Octopus (<i>Octopus rubescens</i>)	+ +		[25]

what extent the concept of coping styles is really related to the individual vulnerability to stress-mediated disease.

This review will discuss these major issues and it will be argued that the clustering of various behavioral characteristics may to some extent be causally related to differences in (re)activity of the neuroendocrine system.

2. Behavioral characteristics of coping styles

Much of our current thinking on coping styles is derived from the work of Jim Henry [10]. He suggested, on the basis of social stress research in animals and man, that two stress response patterns may be distinguished. The first type, the active response, was originally described by Cannon [11] as the fight-flight response. Behaviorally, the active response is characterized by territorial control and aggression. Engel and Schmale [12] originally described the second type of stress response as the conservation-withdrawal response. This response pattern is characterized behaviorally by immobility and low levels of aggression.

Table 2

Summary of the behavioral differences between proactive and reactive male rats and mice

Behavioral characteristics	Behavioral characteristics		References
	Proactive	Reactive	
Attack latency	Low	High	[14]
Active avoidance	High	Low	[70,83]
Defensive burying	High	Low	[84], this paper
Nest-building	High	Low	[85]
Routine formation	High	Low	[16]
Cue dependency	Low	High	[17,84]
Conditioned immobility	Low	High	[17]
Flexibility	Low	High	[77]

These ideas led to the hypothesis that the individual level of aggressive behavior, i.e. the tendency to defend the home territory, is related to the way individual males react to environmental challenges in general. The hypothesis was tested by Benus [13] using male house mice that were genetically selected for either short attack latency (SAL) or long attack latency (LAL). Also when other indices of aggressive behavior are taken into account, the SAL males are considered extremely aggressive whereas the LAL males have very low levels of intermale aggressive behavior [14]. The results of a series of experiments not only in mice, but also in rats, suggest the existence of at least two coping styles, which are summarized in Table 2. We prefer to use the terms proactive coping rather than active coping and reactive rather than passive coping (see further). Several conclusions can be drawn from these results. First, the individual level of aggressive behavior is indeed related to the way in which the animals react to a wide variety of environmental challenges. Second, it seems that aggressive males have a more proactive type of behavioral response, whereas non-aggressive or reactive males seem to be more adaptive and flexible, responding only when absolutely necessary.

An important fundamental question is whether the two types of behavior patterns can be considered to represent styles of coping in the sense that they are both aimed at successful environmental control [15]. Several experiments indicate that the different behavior patterns can indeed be considered as coping styles aimed at environmental control. This is, for example, shown in a recent experiment using wild-type rats. This strain of rats shows a large individual variation in aggressive behavior similar to the variation in wild house mice. After being tested for their tendency to defend the home cage against an unfamiliar male conspecific, the males were tested in a shock prod defensive burying test. In this test, the animal is confronted with a small,

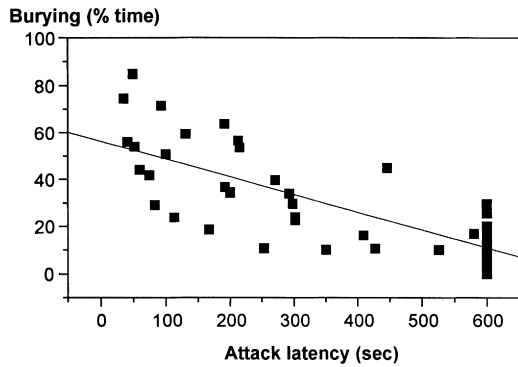


Fig. 1. Correlation ($R = 0.72$) between attack latency score in rats as measured in the resident intruder paradigm and the percentage of time spent burying in the defensive burying test of 10 min duration.

electrified prod in its home cage. Because this prod is a novel object, the experimental animal will explore it by sniffing at the object. Consequently, the animal receives a mild but aversive shock. As soon as it has experienced the shock, the animal has two options to avoid further shocks. It may either hide in a corner of the cage to avoid further contact with the shock prod, or it may actively bury the shock prod with the bedding material of the cage. Under these free choice conditions, aggressive males spend most of the test-time (10 min) burying (Fig. 1) while non-aggressive males show immobility behavior. Notice, however, that the two types of responding are equally successful in avoiding further shocks. In this particular test, successful coping can be defined operationally as avoidance of further shocks. The terms active and passive coping are frequently used to indicate the differences between the two styles. However, these terms may lead to some confusion, because the terms

do not properly describe the fundamental differences. A very fundamental difference seems to be the degree in which behavior is guided by environmental stimuli [16,17]. Aggressive males easily develop routines, i.e. a rather intrinsically driven rigid type of behavior. Non-aggressive males in contrast are more flexible and react to environmental stimuli all the time. For that reason, we prefer to use the terms proactive coping and reactive coping. This differential degree of flexibility may explain why aggressive males are more successful under stable colony conditions, whereas non-aggressive males do better in a variable or unpredictable environment, for example during migration [18].

It is important to emphasize that the differentiation in coping styles may not be expressed equally clearly in all challenging situations. In particular, tests that measure aspects of initiative or proactivity seem to be most discriminative. This holds, for example, for latency measures such as the attack latency test in males or the defensive burying test, which allow the animal a choice between proactive and reactive coping. Although female mice usually do not show territorial aggression, females of the short attack latency selection line show much more defensive burying than female mice of the long attack latency selection line. This supports our view that aggression is only one of a larger set of behavioral characteristics that make up the proactive coping style.

3. Distinct coping styles: distribution and consistency over time

The concept of coping style and the way it is generally

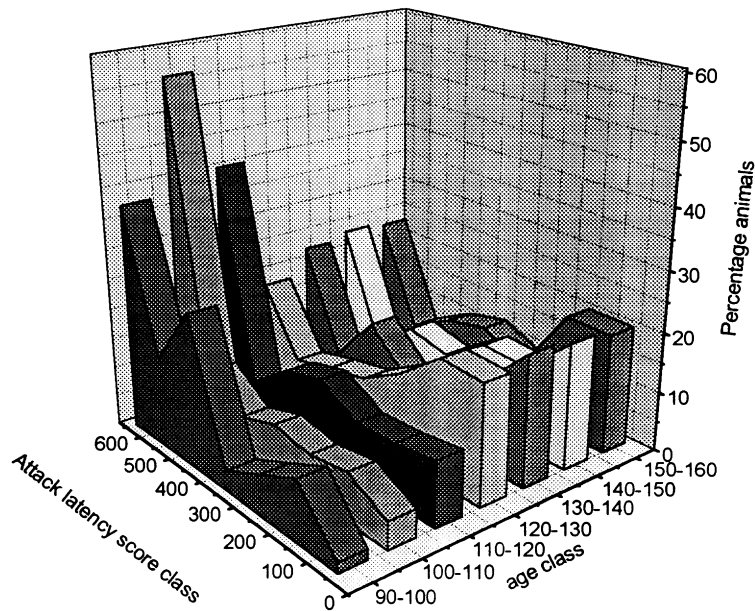


Fig. 2. Frequency distribution of attack latency scores (seconds) obtained in the 5th to the 12th generation of laboratory bred wild-type male rats ($N = 2500$) in different age classes (postnatal days).

presented in the literature suggests that there are distinct phenotypes, which are more or less stable over time in their response to stressors. The early studies by Oortmerssen and colleagues, on a feral population of house mice suggest a bimodal distribution of male phenotypes as measured by the individual latency to attack a standard intruder into the home cage [18]. The idea of bimodal distributions has been strengthened by the fact that the phenotypical differences appeared to have a rather strong genetic component. Genetic selection for either of the extremes of the variation in a certain behavioral or physiological characteristic generally results in distinct genotypes within a few generations. Many studies on coping styles and individual vulnerability to stress mediated disease are based on the use of such genetic selection lines. Selection lines have rather stable characteristics, which are relatively insensitive to environmental influences. However, there is confusion in the literature on this issue, because several investigators using unselected strains of animals were unable to find clearly distinct and stable coping styles. The main problem seems to be the large diversity in origin, age and gender of the experimental animals involved. In the few studies that consider feral populations, distinct phenotypes are found. Both in wild house mice and in a small bird, the great tit (*Parus major*), latency measures seem to have a bimodal distribution [18,19]. However, one has to realize that the distribution is not truly bimodal because latency measures are generally finite, i.e. above a certain time the latency is set to the maximum value. This leads to an accumulation of individual scores in the distribution curve at this maximum value. Nevertheless, the individual behavioral scores in wild populations are certainly not normally distributed. An analysis of a large database of aggressive behavior of a population of 2500 laboratory-bred adult male wild rats reveals an age-dependent change in the distribution of attack latencies. Above a certain age, three peaks emerge in the frequency distribution, with a clear intermediate group (see Fig. 2). This difference with the wild situation may be explained by the fact that there is little or no selection pressure in the laboratory. It is tempting to consider the possibility that intermediate animals are less successful in nature. Few studies address the survival value of distinct proactive and reactive coping styles. However, recent, yet unpublished studies in feral populations of birds indicate that the fitness of different coping styles depends on the stability of the environment in terms of social structure and food availability.

Many studies use laboratory strains of animals or heavily domesticated farm animals like pigs. Usually, individual behavioral scores are normally distributed in these studies. For example, several studies in pigs show that the distribution of individual scores in the back-test is normally distributed [20,21]. Moreover, it is hard to tell how a certain inbred or domesticated strain relates to the original and presumably functional distribution of its wild ancestors. However, it is intriguing that the extremes of this normal distribution still

fulfill the criteria for proactive and reactive coping styles, both behaviorally and physiologically [20]. Although the discussion on the shape of the distribution curve is important from an evolutionary point of view, it does not seem to matter much when individual vulnerability to stress-related diseases is concerned. After all, it has been repeatedly shown that the extremes in a population, irrespective of the detailed distribution curve, may differ not only quantitatively, but also qualitatively in their behavioral and physiological response pattern to stress (see Table 1). Evidence has been found in different species that the behavioral and physiological response of individual animals to a specific stressor is consistent over time. In pigs, for example, individual gilts that displayed relatively long latency times to contact a novel object and spent relatively little time near the object during their first exposure showed a similar response when re-tested one week later [22]. Also in dairy cows, consistency was measured in behavior, in heart rate and in plasma cortisol concentrations when individual animals were repeatedly tested in a novel environment test over one week. Moreover, consistent stress responses to the same test were also found for cardiac and adrenocortical responses over one year [23].

Another important issue concerns the one-dimensional character of the concept of coping styles. Several studies have used a factor analytical approach to reduce the sources of individual variation in a population to a limited number of components [24–26]. This statistical approach usually reveals two or three factors that explain a considerable part of the individual variation. Although some of these factors relate to trait characteristics or aspects of personality similar to coping styles, others may relate to state variables such as stress and fear. These studies, both in humans and in animals, emphasize the multidimensional character of individual (personality) traits. However, aspects of aggression such as hostility, impulsivity, anger or proactivity are often found as an important dimension. In an experimental study in Roman High and Roman Low avoidance lines of rats, Steimer et al. [27] includes the dimension of emotional reactivity as a second trait characteristic. By correlating behavior of individual animals in a number of coping style and emotion/anxiety related tests, he found evidence for two independent dimensions, i.e. coping style and emotional reactivity. Individual behavioral profiles calculated either on indices of emotional reactivity or on indices of exploratory activity as an indirect measure of coping style resulted in different clustering of individuals. These two dimensions together might explain individual vulnerability to anxiety.

4. Neuroendocrine characteristics of coping styles

Differences in coping style have been observed in male rodents during both social and non-social stressful conditions (see Table 2). Coping styles are not only characterized

Table 3
Summary of the physiological and neuroendocrine differences between proactive and reactive animals

Physiological and neuroendocrine characteristics			
	Proactive	Reactive	References
HPA axis activity	Low	Normal	[33,38,56,70,86]
HPA axis reactivity	Low	High	[20,28,56,87]
Sympathetic reactivity	High	Low	[38,77,88]
Parasympathetic reactivity	Low	High	[37,39]
Testosterone activity	High	Low	[34,35]

by differences in behavior but also by differences in physiology and neuroendocrinology. As mentioned earlier, tests that measure aspects of initiative or proactivity seem to be most discriminative. The defensive burying tests in rodents is such a test, which allows the animal a choice between proactive and reactive coping. In general, defensive burying is accompanied by high plasma noradrenaline and relatively low plasma adrenaline and corticosterone, while freezing behavior is associated with relatively low plasma noradrenaline and high plasma corticosterone levels [28,29]. In a strain of wild-type rats, the more aggressive males showed the highest levels of burying behavior and showed a larger catecholaminergic (both plasma noradrenaline and adrenaline) reactivity after electrified prod exposure and after social defeat than did the non-aggressive rats [30]. Previously, it was shown that during social defeat the more competitive proactive male rats reacted with higher responses of blood pressure and catecholamines than the more reactive rats. In addition, these competitive males had higher baseline levels of noradrenaline [31]. The same holds for strain differences. The aggressive Wild type-rats responded to social defeat with larger sympathetic (plasma noradrenaline levels) reactivity and concomitantly lower parasympathetic reactivity (as measured by increased heart rate response and decreased heart rate variability) than the less aggressive Wistar rats [32]. Thus, proactive coping rodents show in response to stressful stimulation a low HPA-axis reactivity (low plasma corticosterone response), but high sympathetic reactivity (high levels of catecholamines). In contrast, reactive coping rodents show higher HPA axis reactivity and higher parasympathetic reactivity (Table 3).

Differences in endocrine activity have also been observed for HPA axis and gonadal axis activity under baseline conditions. In aggressive mice, reduced circadian peak plasma corticosterone levels have been observed as compared to non-aggressive mice [33]. In mice of the short attack latency selection line and in wild-type male rats, high baseline levels of testosterone have been observed [34,35].

There is a growing body of evidence that similar coping styles can be found in farm animals as well. Hessing and colleagues showed that male castrated pigs could be characterized as high resistant or low resistant at an early age (1–2 weeks) by means of a back-test (manual restraint) [36]. In this back-test, a piglet is put on its back and the number of

bouts of resistance is used to characterize the animal. The high-resistant pigs made more escape attempts and mean heart rate frequency was higher than in low-resistant pigs [36]. At three and at eight weeks of age, the high-resistant ones were less inhibited in approaches to novel objects in an open field. But the high-resistant pigs spent less time in exploring the novel object than low-resistant pigs [36]. Heart rate frequency of high-resistant pigs was also substantially increased in reaction to a falling novel object, while heart rate frequency of low-resistant animals was only slightly increased or even decreased (bradycardia), suggesting that parasympathetic reactivity was higher in low-resistant pigs [37]. Hessing and colleagues did not find clear differences in HPA axis reactivity between the high- and low-resistant animals, although basal plasma cortisol levels were higher in low-resistant than in high-resistant pigs and this was accompanied by adrenal hypertrophy. Recently, however, Ruis et al. [20,21] showed clear differences in HPA axis reactivity in high- and low-resistant female pigs. The low-resistant animals had higher HPA axis reactivity than the high-resistant ones. This was shown by higher salivary cortisol responses to a novel environment test, to routine weighing at 25 weeks of age, and to administration of a high dose of ACTH [20]. Interestingly, the low-resistant animals with high HPA axis reactivity at 24 weeks of age, showed less aggression in group-feeding competition tests, hesitated longer to leave their home pens and to contact a human than did high-resistant animals. Altogether, pigs that showed high resistance in the back-test and low HPA-axis reactivity and high sympathetic reactivity in response to stressful stimulation are thought to be representatives of the proactive coping style. In contrast, pigs that showed low resistance in the back-test and high HPA axis reactivity and high parasympathetic reactivity are thought to be representatives of the reactive coping style.

Recently, it was shown that laying hens, from two lines with high or low propensity to feather peck, also show individual differences in physiological and behavioral responses to stress that are similar to the described coping styles. During manual restraint (keeping the bird on its side by hand for 8 min), the high feather pecking line showed more resistance and higher mean heart rate frequency and lower parasympathetic reactivity than the low feather pecking line [38,39]. HPA axis reactivity (plasma corticosterone levels) was highest in the low feather pecking line, while the sympathetic reactivity (plasma noradrenaline levels) was the highest in the high feather pecking line. These data suggest that chickens of the high feather pecking line are representatives of the proactive coping style, whereas birds of the low feather pecking line are representatives of the reactive coping style.

5. Causal relationship between neuroendocrine and behavioral characteristics of coping

One may wonder to what extent the behavioral and

physiological characteristics are causally related. Of course, it is highly unlikely that all differences in coping style can be reduced to one single causal factor. However, evidence is accumulating that a differential HPA axis reactivity may explain some of the behavioral differences. In different species, freezing behavior as part of the reactive coping response can be observed in response to an inescapable stressor or predator. In rats, a large number of studies have shown that corticosteroids play a permissive role in this fear-induced freezing behavior. Adrenalectomy (ADX) impaired the duration of fear-induced freezing compared to sham-ADX controls, suggesting the involvement of adrenal hormones. This behavioral deficit in ADX animals could be restored by the application of corticosterone [40]. In line with these experiments, treatment with metyrapone, a corticosteroid synthesis inhibitor, reduced fear-induced freezing behavior, suggesting that corticosterone is a key hormone in the expression of fear-induced immobility [41]. Since corticosterone can bind to both the mineralocorticoid and glucocorticoid receptor, further experiments were performed to find out which specific receptor type was involved. Intracerebroventricularly administered mineralocorticoid receptor antagonist RU28318 reduced the fear-induced freezing response, whereas the glucocorticoid receptor antagonist RU38486 was without effect [42]. The modulation of freezing via a mineralocorticoid receptor-dependent mechanism did not come as a surprise. Limbic mineralocorticoid receptors bind corticosterone with about 10 times higher affinity than glucocorticoid receptors, and low circulating levels of the corticosteroid hormone almost completely occupy mineralocorticoid receptors [43,44]. The biological background could be that a glucocorticoid receptor-dependent mechanism would have been too slow because glucocorticoid receptors are only occupied at much higher hormone levels that are reached several minutes after the stressor. In nature, the permissive steroid mineralocorticoid receptor action makes an immediate freezing response possible during a sudden appearance of a predator. There is a growing body of evidence that corticosteroids also play a role in fear-induced behavioral inhibition in farm animals. In laying hens, it has been shown that the birds with the shortest tonic immobility response have the lowest corticosterone levels [45]. Further, chronic administration of corticosterone moderately increased plasma levels of corticosterone and prolonged the tonic immobility reaction in hens suggesting a causal role for corticosteroids [46]. Also, in dairy calves, a positive correlation was observed between plasma cortisol levels and the latency to approach a novel object (van Reenen, unpublished observation).

6. Coping styles and differences in disease vulnerability

The concept of coping styles implies that animals have a differential way to adapt to various environmental conditions. Negative health consequences might arise if an animal

cannot cope with the stressor or needs very demanding coping efforts. Sustained over-activation of various neuroendocrine systems may lead to specific types of pathology. Hence, in view of the differential neuroendocrine reactivity and neurobiological make-up, one may expect different types of stress-pathology to develop under conditions in which a particular coping style fails. Although there are only a limited number of studies performed concerning pathology in relation to the type of coping style adopted, there are some indications that the two coping styles differ in susceptibility to develop cardiovascular pathology, ulcer formation, stereotypies and infectious disease.

6.1. Cardiovascular disease

Various studies emphasize the differences between the two coping styles in autonomic balance. Because of the role of the two branches of the autonomic nervous system in cardiovascular control, one may expect in conditions of over-activation of these systems, a differential vulnerability for various types of cardiovascular pathology as well. Indeed, a number of experiments found evidence that the proactive coping animal is more vulnerable to develop hypertension, atherosclerosis and tachyarrhythmia due to the high sympathetic reactivity [32,37,47–49]. However, hypertension has never been observed after conditions of uncontrollable stress. In social groups, hypertension generally develops in dominant or subdominant males that have difficulties to maintain their social position. Therefore, it seems that these types of cardiovascular pathology only develop under conditions of threat to control rather than loss of control [15]. The reactive coping style seems to be characterized by a shift in the autonomic balance towards a higher parasympathetic tone and reactivity as can be observed by a strong bradycardia response in reaction to a sudden unpredicted stressor. Although there have been no systematic studies of the cardiovascular consequences of this characteristic, one may suggest that these types of animals are more vulnerable to sudden cardiac death due to bradyarrhythmia.

6.2. Gastric ulceration and stereotypies

There are numerous studies to indicate that the controllability of stressors is an extremely important factor in ulcer formation. The development of ulcers is low when animals are able to actively control or predict the stressor or divert their attention away from the stressor. For example, if rats can terminate the inescapable shock, or can chew wood during inescapable shock [50], or can bite on a wooden stick during cold restraint stress less, ulcers are observed [51].

The classical studies of Weiss [50] showed that the development of ulcers was high when the number of active coping attempts was high in the absence of informational feedback or with negative informational feedback present. In the experimental animal that could actively control the

aversive shock by either pressing a lever during the warning signal or during the shock itself, the total length of stomach wall erosions was much smaller than in the yoked partner, which received exactly the same number of shocks, but could not control them. Also, when a feedback tone was given after each correct avoidance–escape response, the amount of gastric ulceration was further reduced. However, when brief punishment shock was given to the avoidance–escape and yoked animals whenever an avoidance–escape was made, then the avoidance–escape group showed more severe ulcer formation than the yoked partners. Further, in the absence of informational feedback, a positive correlation was observed between the number of active coping attempts and the amount of gastric ulceration.

In line with these results is an observation in Roman high avoidance (RHA) and Roman low avoidance (RLA) rats, which can be considered to represent the proactive and reactive coping style, respectively. It was shown that RHA rats, after stress of food-deprivation for five days, had more stomach lesions than RLA rats [52]. A negative correlation between attack latency in the intruder test and gastric ulceration induced by restraint-in-water stress [53], also suggests that animals that prefer a proactive coping style are more vulnerable to the formation of ulcers during uncontrollable stress. In rat colonies, dominant animals that are usually representatives of the proactive coping style are reported to develop stomach wall erosions when they have lost their leading position (social outcast) after frequent attacks by other colony members [15].

Another example of a possible relationship between behavioral coping characteristics and pathology has been found in veal calves. It was shown that veal calves fed only with milk developed tongue-playing as a stereotypy [54]. However, not all calves did this with the same intensity. Those calves that developed a lot of oral stereotypies showed less stomach wall ulcers when slaughtered at 20 weeks of age. However, calves that did not develop tongue-playing, all had such ulcers at the same slaughter age [54]. Recently these results were confirmed in a larger study involving 300 veal calves (van Reenen et al., in preparation). Also in tethered breeding sows that were housed individually, two separate groups could be distinguished: some cows spent up to 80% of their active time in this behavior while others hardly developed stereotypies. Surprisingly, the sows that showed less initial resistance in the back-test were the ones to develop high levels of stereotypy later on [55]. Recently, it was shown that high levels of stereotypies are associated with a reduced sympathetic activation caused by the chronic stress of tethering as was shown by a decrease in heart rate during bouts of stereotyped behavior. In this view, stereotypies help the animal to cope with the adverse situation of tethering [56].

There is increasing evidence that individual animals that adopt the proactive or reactive coping style differ in sensitivity of the dopaminergic system and consequently they may differ in vulnerability to the development of

stereotypies. For instance, in mice, the dopamine receptor agonist apomorphine produced a greater enhancement of stereotyped behavior in proactive coping animals than in reactive coping animals, suggesting that proactive coping animals may be associated with a more sensitive dopaminergic system [57]. Similar correlations were found in rat lines previously selected for high and low expression of stereotyped behavior (gnawing) in response to apomorphine. The apomorphine-susceptible rats showed more proactive coping behavior (fleeing), whereas the apomorphine-unsusceptible rats showed more reactive behavior (freezing) in reaction to an open-field [58]. A similar relation between coping style and stereotypy has been demonstrated in pigs. Individual proactive (high resistant) and reactive (low resistant) coping pigs can be distinguished in the back-test in which the reaction to manual restraint is measured [59]. Recently it was shown that the high-resistant pigs have a higher oral stereotypic response (snout contact-fixation with floor) to apomorphine as compared to low-resistant pigs [60]. Thus, also in pigs there is a relationship between coping style, sensitivity of the dopaminergic system and development of stereotypies. Moreover, it has been shown that the dopaminergic-sensitivity factor, i.e. the latency to initiate stereotypic gnawing induced by apomorphine, also predicted ulcerogenic vulnerability [61].

The underlying mechanism of increased vulnerability of proactive coping animals to develop stereotypies is not well understood. Here it is hypothesized that altered HPA-axis regulation plays a crucial role in the development of stereotypies. In farm animals it has been suggested that stereotypies are performed to lower the state of arousal and anxiety and to lower corticosteroid levels; however, not all studies show this correlation [62]. A possible explanation for the conflicting data may be the differential effects of corticosteroid hormones at the stage when the stereotypy starts to develop and at the stage when a full-blown stereotypy continues to exist. It is hypothesized that stress levels of corticosteroids may enhance the acquisition and expression of stereotypies, whereas an already developed stereotypy may reduce corticosteroid levels. This is supported by the following two examples in rodents. First, amphetamine activates dopamine pathways and induces stereotyped behavior (e.g. gnawing) that can be potentiated by high levels of corticosterone [63]. This suggests that brain glucocorticoid receptors are involved. Moreover, corticosteroids sensitize the dopaminergic system, probably through binding to the glucocorticoid receptors [64]. Second, dopamine-depleting lesions of the caudate-putamen are associated with a reduction in stereotyped behavior but an enhanced corticosterone response [65]. Thus, glucocorticoids via glucocorticoid receptors may play an important role in the sensitization of the dopaminergic system. Interestingly, apomorphine-susceptible rats do differ in glucocorticoid receptor and mineralocorticoid receptor expression in different brain nuclei and have higher (and more prolonged) plasma ACTH and total plasma corticosterone responses than

apomorphine-unsusceptible rats [58]. Further studies are needed to investigate whether these differences in corticosteroid receptor expression are responsible for the differences in sensitivity in the dopaminergic system and whether this is the underlying mechanism which, under conditions of severe stress, increases the vulnerability of the proactive coping animal to develop stereotypies.

6.3. Immunological defense during coping or non-coping

Contemporary psychoneuroimmunology emphasizes the role of the HPA axis and the sympathetic branch of the autonomic nervous system in communication between the brain and the immune system [66]. In view of the differential reactivity of these two systems in the two coping styles, one may expect to see differences in the immune system as well. Indeed, several studies in rats and mice demonstrate that individual differentiation in coping is an important factor in stress and immunity. In the social stress models in particular, the individual level of social activity seems to be an important explanatory variable in some studies [67,68]. Although these studies do not specifically address the issue of coping styles, it is tempting to consider the possibility that these socially active animals represent the proactive coping style. Sandi et al. [69] specifically addressed the question of the significance of individual differentiation in emotional responsiveness to the differentiation in immunology. They used the Roman-high (RHA) and low-avoidance (RLA) rats that have been genetically selected on the basis of their active avoidance behavior [70]. These selection lines have been shown to differ in a number of behavioral and neuroendocrine stress responses in a similar way as the proactive and reactive coping styles mentioned above. It was shown that the NK cell activity and the proliferation response of splenocytes to mitogenic stimulation was lowest in the RLA males, a difference that was even more pronounced after the stress of active shock-avoidance learning. Other evidence that emotionality may interact with the immunological response has been found in dairy cows. During endotoxin mastitis in cows that were socially isolated, animals that were selected one year earlier for a strong adrenocortical response to isolation, showed a significantly larger reduction in peripheral blood lymphocyte numbers than cows that were previously classified as weak responders [71].

In a study of pigs, Hessing [72] demonstrated that aggressive, resistant pigs had a higher *in vivo* and *in vitro* cell mediated immune response to specific and non-specific antigens than non-aggressive, non-resistant pigs. After stress, the aggressive, resistant pigs showed the strongest immunosuppression. This difference in immunological reactivity in relation to coping style may explain the differential disease susceptibility associated with social rank in group-housed pigs after challenge with Aujeszky virus. These observations in pigs are consistent with similar data obtained in colony housed male rats [67]. Finally, a recent observation

shows that proactive coping male rats are more vulnerable to the experimental induction of the autoimmune disease EAE (experimental allergic encephalomyelitis), which is considered to be an animal model for multiple sclerosis in humans. This high vulnerability seems to be due to the high sympathetic reactivity in the proactive coping males [73].

7. Concluding comments

The concept of coping style has been frequently used in many studies and in an increasing number of species. However, only a few studies have a sufficiently broad approach to the individual behavioral and physiological characteristics and their consistency over time to be conclusive on the generality of the typology across species. Nevertheless, the available literature makes it tempting to consider the possibility that the distinctions between proactive and reactive coping styles represent rather fundamental biological trait characteristics that can be observed in many species. Species or strains may differ in their degree of differentiation depending on the strength of the selection pressure in nature or in the laboratory (genetic selection, domestication), but the extremes within a certain population differ generally in the same behavioral and physiological parameters and in the same direction. This may be partially due to the possibility that some of the characteristics share a common causal physiological basis. The few studies in feral populations suggest that the individual differentiation in coping style may be highly functional in population dynamics. Phenotypes within one species seem to have a differential fitness depending on the environmental conditions such as population density, social stability, food availability, etc. This idea is strengthened by the ecological studies of Wilson and co-authors [74,75]. Although these authors use the term shyness and boldness to indicate individual differences within a population, they argue that this differentiation represents adaptive individual differences in resource use and response to risk.

Different coping styles are based on a differential use of various physiological and neuroendocrine mechanisms. The general impression is that these mechanisms vary in the same direction consistently over species. However, the degree of variation and the organizational level at which the variation is expressed may differ. It is likely that genetic selection will artificially exaggerate trait characteristics up to a level, which may not normally be found in a natural population. There are certainly more dimensions that may account for the individual differentiation in behavior and physiology. It will be a major challenge for behavioral physiologists to refine the scales for individual differences in order to improve their predictive power for health, welfare and disease.

Little is currently known about the origin of coping styles. The few genetic selection lines that have been sufficiently characterized both behaviorally and physiologically

indicate a strong genetic basis. Some recent studies suggest that perinatal factors might play a role as well. However, the use of genetic selection lines may overestimate the role of the genotype. Indeed, the fact that cross-fostering and embryo transfer did not affect aggressive behavior in our selection lines of mice indicates that these lines are devoid of any perinatal plasticity [76]. Unfortunately, the large number of recent studies on the influence of perinatal factors in adult stress-reactivity rarely considers a sufficiently wide spectrum of behavioral and physiological characteristics to be conclusive on the effects on coping styles as a coherent set of characteristics. The same holds for the influence of adult (social) experiences. Clearly, stress at an adult age may produce enduring changes in behavior and physiology. Whether it changes coping styles as a trait characteristic is virtually unknown. So far, we prefer to consider coping styles as rather stable trait characteristics originating from genetic factors in combination with epigenetic factors early in life. Experiences in adult life may alter the state of the animal for a long period of time as expressed in some behavioral and physiological parameters, but they do not seem to change the coping style as a whole. In contrast, coping style is not a rigid characteristic that allows the individual only to respond according to one specific coping style in all situations. The absence of sawdust in the defensive burying test, for example, also elicits freezing behavior in the proactive animal. In this case, the environment was restrictive and consequently the animal did not follow its preferred coping style.

The available evidence so far confirms the idea that coping style helps to determine individual vulnerability for stress-related disease. First, the concept implies that animals may be differentially adapted to different environmental conditions. Second, the differences in physiological reactivity make the two coping styles vulnerable to different types of disease. Hence, in our view, psychopathology can only be understood as a function of the individual coping style and the environmental demands. Understanding this complex relationship is of crucial importance in understanding human and animal health and welfare.

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