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Review

Pathological anxiety in animals

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Abstract

Selective breeding programmes in domestic and laboratory animals generally focus on physiological and/or anatomical characteristics. However, selection may have an (unintended) impact on other characteristics and may lead to dysfunctional behaviour that can affect biological functioning and, as a consequence, compromise welfare and quality of life. In this review it is proposed that various behavioural dysfunctions in animals are due to pathological anxiety. Although several approaches have been undertaken to specify the diagnostic criteria of pathological anxiety as a behavioural disorder in animals, the causal aetiology largely remains unknown. This is mainly due to the fact that integrated concepts, combining the behavioural syndrome and (neuro-) physiological processes, are widely lacking. Moreover, even the term anxiety itself represents a poorly defined concept or category. A definition is suggested and the potential causes of pathological anxiety are explored with a plea for developing adequate diagnostic tools and therapies to fight pathological anxiety in animals based on insight from scientific research.
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1. Introduction to the problem

Behavioural dysfunctions can compromise biological functioning and as a consequence impair welfare and quality of life in pet, farm and laboratory animals. Society's concern about the welfare of the compromised animal is growing. While veterinarians are increasingly confronted particularly with problems associated with behavioural dysfunctions in pet animals, diagnosing and treating these syndromes remains difficult since scientifically based knowledge on both the aetiology and nature of behavioural dysfunctions is poor. Even more, this lack of knowledge holds true for all groups of animals kept by man (pet, farm and laboratory animals), albeit to a varying degree.

Domesticated animals are bred to meet specific demands of their owners. Selection criteria generally focus on physiological/anatomical characteristics such as visual appearance in pet animals as defined by breed standards, productivity in farm animals (Grandin and Deesing, 1998), or reproducibility and ease of handling in laboratory animals. For dogs, these standards are specified by the Fédération Cynologique Internationale (FCI). Likewise, breeding standards for horses are defined by different independent national and international organizations. Many breed standards over the decades have changed from their initial intention to provide a description of the unique qualities of breeds to the definition of a "blueprint" for breed (type) consistency (Brackman, 2001), finally resulting in a rigid adherence to breed standards. This may freeze behavioural deficits in breeds.

In laboratory animals, highly specific characteristics are genetically selected or genetic modifications are conducted, often ignoring the possibly complex consequences of such processes. Genetic alterations will often affect behaviour as well. While some behavioural alterations facilitate the interaction between domestic animals and humans, for example a decreased flight-distance and increased timidity,

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others, such as increased aggressiveness, may seriously disturb this interaction. Most behavioural alterations resulting from selective (in-)breeding are, however, less prominent and are not even being recognised.

One of the consequences of (in)breeding is that the biological variability of the species will narrow down, possibly leading to a significant reduction of behavioural flexibility. Such alterations will be manifest as behavioural dysfunctions when environmental conditions extend an individual's adaptive capabilities. We propose that various behavioural dysfunctions of pet, farm, and laboratory animals are an expression of pathological anxiety.

2. Definition of pathological anxiety

Anxiety is an essential emotion, which is highly conserved during evolution. Emotions may have evolved because they coordinate response systems, and prepare the organism to face challenges (Gross, 1999). They are a component of an animal's normal repertoire to cope with, for example, (potentially) dangerous situations. In principle, anxiety is an adaptive reaction when an animal is confronted with potential danger or threat (Marks and Nesse, 1994; Boissy, 1995; Rosen and Schulkin, 1998).

Behavioural and physiological responses accompanying anxiety prepare an individual to react appropriately, for instance by displaying defensive or offensive behaviour. Thus, anxiety enables an individual to escape from danger and to avoid it in the future, i.e. to adapt to environmental challenges (Livesey, 1986). If anxiety-responses are inappropriate, the individual's ability to adapt to environmental conditions will be substantially compromised.

In interaction with cognitive processing, anxiety regulates behaviour in humans and other animals. The assessment of anxiety-related behaviour in animals is based on the assumption that their anxiety is comparable to that in humans. In fact, it cannot be proven that an animal experiences anxiety in the same way as does a human being. However, it is undisputed that distinct behavioural and physiological patterns in animals indicate anxiety, i.e. physiological and behavioural changes (see Table 1) known to accompany high sympathetic nervous activity (Hall, 1936). From this, an analogy, if not a homology, between (normal) anxiety in humans and rodents can be assumed (Lang et al., 2000).

In humans, pathological anxiety is characterized by excessive anxiousness and worry (apprehensive expectation about a number of events or activities, such as work or school performance) and occurring for at least six months. *The Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV, 1994) describes 12 different anxiety disorders. Their nosology, however, is unsuited to diagnose anxiety in animals. It is, for example, impossible to obtain evidence about 'apprehensive expectations' in animals. Even worse, the term 'anxiety' itself represents a poorly defined concept or category (Friman et al., 1998).

Table 1
Examples of physiological and behavioural signs of anxiety (see, for example Boissy, 1995; Lang et al., 2000)

Physiological signs of anxiety	Behavioural signs of anxiety
Tachycardia, bradycardia, elevated BP	Freezing, tonic immobility, increased ambulation
EEG arousal	Panting
HPA axis reactions, corticosteroid release	Behavioural arousal, irritability, restlessness
Muscle tension	Facial expressions of anxiety
Pupil dilation	Urination, defecation
	Aggression, threatening behaviour
	Increased vigilance/attention
	Sleep disturbances

Abbreviations: BP, blood pressure; HPA, the hypothalamic–pituitary–adrenal axis; EEG, electroencephalogram.

In order to obtain a theoretical basis for studying anxiety, and in particular pathological anxiety in animals, we must step back to a more biologically fundamental definition (see also Rosen and Schulkin, 1998). In fact, even animal models for pathological anxiety in humans are referred to as showing 'high' or 'extreme' anxiety (Escorihuela et al., 1999; Landgraf and Wigger, 2002). There is, therefore, an urgent need for systematic approaches to define and characterise "pathological anxiety" in animals. The physiological and behavioural responses and the proximity of anxiety-inducing stimuli can be used to define anxiety.

We suggest the following definition:

> Pathological anxiety is a persistent, uncontrollable, excessive, inappropriate and generalized dysfunctional and aversive emotion, triggering physiological and behavioural responses lacking adaptive value. Pathological anxiety-related behaviour is a response to the exaggerated anticipation or perception of threats, which is incommensurate with the actual situation.

With this definition, we are not trying to translate the different diagnoses of anxiety disorders in humans (as defined in, for example, DSM-IV, 1994) to different anxiety states in animals. Rather, we are attempting to summarise anxiety, which appears to lack adaptive value and severely interferes with normal (i.e. adaptive) interaction of the sufferer with its physical and social environment, under the concept of "pathological anxiety".

3. Possible causes for the development of pathological anxiety: Genes, epigenetics and environment

Multiple factors affect the development of emotional behaviour. A conceptual scheme by Ingram and Kendall (1987) may be useful to differentiate between the components of psychopathologies such as pathological anxiety, which are held responsible for its expression. This phenotype may be broken down in features that are unique to the disorder, components that are common to many different psychopathologies, and components that represent the unpredictable individual differences. Whereas many of the common factors have already been identified, this is not true for the unique, critical features of pathological anxiety. Individual, idiosyncratic events may have been crucial in developing pathological anxiety and their recognition may be of significance for diagnosing this pathology and formulating a therapeutic strategy (Lang et al., 2000).

The genetic background of an individual may be causal for behavioural dysfunctions (see Fig. 1, upper part). More often, genes modulate the individuals' susceptibility to environmental factors (Veenema et al., 2003). The genetic component is highly complex, as a number of (interacting) genes may be involved in the regulation of pathological anxiety and its behavioural expression (Clement and Chapouthier, 1998). Furthermore, one set of genes may act on several behavioural functions, and/or many genes may only have small effects on the trait under study. These may be reasons for the limited success in identifying gene loci and fine-mapping of the genes involved in complex behavioural dysfunctions (Gershenfeld and Paul, 1997) such as pathological anxiety.

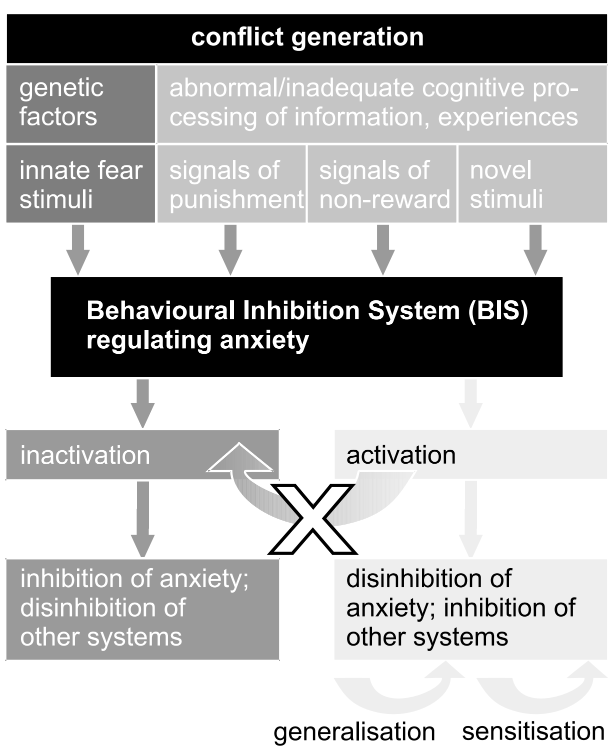

Fig. 1. The behavioural expression of anxiety is regulated by the central nervous behavioural inhibition system (BIS, McNaughton and Gray, 2000). If a conflict is cognitively processed, the BIS will activate/inactivate motivational systems, including anxiety. The more anxiety is activated, the more other motivational systems will be inhibited and vice versa. The balance between activation and inactivation of anxiety is depending on the adaptive capability of an individual. A lack of adaptation can lead to either sensitisation (one specific stimulus acts increasingly aversive) towards aversive stimuli based on the over-activation of the behavioural inhibition system or generalisation (stimuli are generally perceived as being aversive) of stimuli due to insufficient activation of the same system. Such a development may finally result in pathological anxiety.

Environmental conditions or interactions with conspecifics or representatives of a different species that are perceived aversive are likely to be decisive for the development of (pathological) anxiety (Boissy, 1995). Although environmental conditions nowadays are partially defined with respect to species-specific demands and human-based husbandry-criteria (e.g. productivity, visual appearance, etc.), they often challenge the adaptive capabilities of husbandry-animals to its utmost. Genetically based increased stress-susceptibility (Dirks et al., 2002; Schmidt et al., 2002) is likely to result in behavioural disorders if the susceptible animal is challenged by highly aversive events during early life, such as maternal deprivation or extremely uniform, i.e. non-stimulating environments.

The unpredictability of environmental factors, or of (aversively perceived) life events is also a central feature in the development of behavioural dysfunctioning. This concept was introduced by Overmier and Seligman (1967). It is based on the observation that animals developed behavioural deficits as a consequence of exposure to stressors such as uncontrollable electric foot shocks. As first shown by Weiss (1968), rats exposed to uncontrollable shocks showed significant weight loss due to decreased food and water intake. Moreover, these animals showed inappropriate coping behaviour and revealed altered sleep patterns as well as a weakened response to previously rewarding brain stimulation, i.e. anhaedonia (Henn et al., 1985; Weiss, 1991). Importantly, these changes were not observed in animals that received the same aversive stimuli but could control their duration.

Unpredictability is unlikely to be of high relevance for farm animals, since environmental conditions involve routine-procedures, which are dedicated to obtain optimum productivity. In contrast, pet animals are often confronted with unpredictable and uncontrollable major life events, such as changes in the social core group (e.g. children leaving the house, babies being born, divorce, etc.), changes in physical environment (e.g. moving to another place), or both. It can be hypothesised that unpredictable major life events more often happen to emotionally vulnerable individuals since these are more frequently difficult to handle, and as a consequence they change hands repeatedly, i.e. are being resold or given to a new owner. The same is true with, for example, horses and dogs with gross behavioural dysfunctions such as increased (pathological) anxiety.

Due to the individual life history of pet animals and horses, respectively, it remains highly difficult, if not impossible, to distinguish between genetic background and environmental factors as being decisive for the development of (potentially) pathological anxiety. There is ample scientific evidence that genetic factors and environmental factors interact in a complex fashion (Clement et al., 2002). More systematic research is needed to build up clear evidence about the mere effects of genetic background and environmental factors as well as their interplay in the development of pathological anxiety.

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4. Fear and anxiety

Anxiety has been characterized as a response to *potential* danger (Chatherall, 2003), as generalized distress (Lang et al., 2000), i.e. as independent from a specific stimulus, whereas fear has been characterized as a response to present danger (Catherall, 2000), in other words, as stimulus or cue-specific (Davis, 1998; Lang et al., 2000). Fear primes the organism to act reflexively in response to these stimuli or cues. The primary locus of control appears to be subcortical structures such as the amygdala that activates hypothalamic nuclei that activate the sympathetic autonomic nervous system and the hypothalamic–pituitary–adrenal axis. In parallel, higher brain regions such as the hippocampus and the cerebral cortex may be activated (''bottom-up'', Chatherall, 2003; see also Davis, 1998; Lang et al., 2003). However, almost all activated neuronal capacity is focused toward the immediate threat, severely interfering with normal processing of information (Chatherall, 2003).

Anxiety elicits behaviours that enable the animal to approach the source of (perceived) threat (McNaughton and Corr, 2004) by increasing attention and stimulating risk assessment (Lang et al., 2000; Blanchard and Blanchard, 1989). The frontal cortex is the primary locus of control; it processes the perceived threat cognitively, and is able to modulate and steer lower levels of neuronal processing (''top-down'', Chatherall, 2003; see also Davis, 1998; Lang et al., 2003). In particular, risk assessment may be distorted in anxiety. It has been speculated that an anxiety-driven hyper-activity of the hippocampus, which has a central role in cognitive processing and inhibitory functions, may have a central role in disturbed cognition (McNaughton, 1997). Fig. 2 depicts the distinction between fear and anxiety schematically, based on the proximity and specificity of the threatening stimuli, and on the primary locus of control (subcortical vs. cortical).

The pathological variant of fear would be phobia, while dysfunctional anxiety would grow out into generalised anxiety disorder. The common characteristic is that pathological variants of fear/anxiety often are acquired, probably as a consequence of cognitive distortions or dysfunctions (Ingram and Kendall, 1987; McNaughton, 1998). The role of cognition in (pathological) anxiety will be addressed below.

Unfortunately, we are still far from being able to define the exact border between normal (but probably extreme) anxiety and pathological anxiety. Expressing exaggerated or unnecessary anxiety in a particular set of circumstances may fall within the normal range (Nesse, 1999). Notably, the diagnosis of, for example, separation anxiety in dogs as a clinically relevant syndrome exclusively focuses on symptomatology, rarely asking for the biological relevance of the observed behaviour (see Table 1 in Appleby and Pluijmakers, 2003). In fact, it may well be possible that the behaviour of the dog is more or less adequate for that spe-

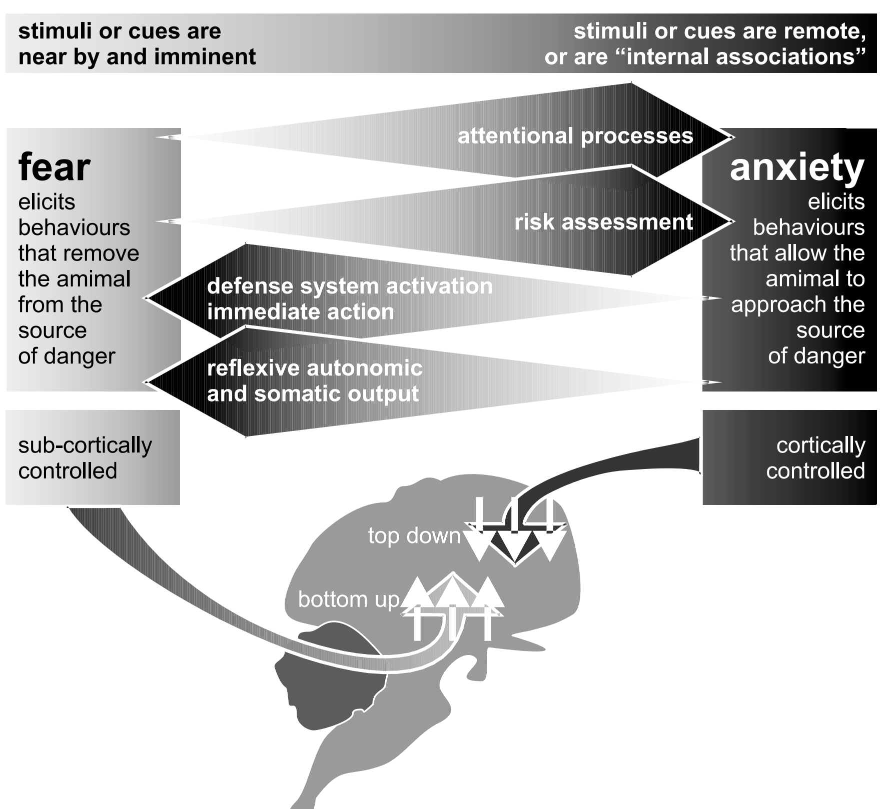

Fig. 2. Distinction between fear and anxiety, based on the proximity of the (perceived) threatening stimuli or cues and the level of cortical control.

cific situation, with the environmental conditions being inadequate. Clarifying this question, however, is essential for developing successful therapeutic strategies.

5. Identification of pathological anxiety

Anxiety is not a unitary phenomenon as it includes innate (trait) anxiety, which is considered to be an enduring feature of an individual, and situation-evoked or experience-related (state) anxiety. State anxiety reflects the response to an anxiogenic stimulus, whereas trait anxiety is considered as an enduring characteristic of an individual (Beuzen and Belzung, 1995). Tests for anxiety in animals are almost always restricted to the evaluation of situation-evoked behaviour, and it might be difficult to investigate trait anxiety in animals. However, both phenomena are not easily separable from each other, as individuals with high trait-anxiety will often show an increased tendency to display high state anxiety as well.

Identifying anxiety in animals is critically dependent on the test methods used. Reliable identification of anxiety requires the implementation of biologically relevant behavioural testing procedures. The minimum requirement for testing anxiety is to allow the animal to display its natural anxiety-related behaviours. It is also important to take into consideration behavioural systems related to anxiety such as, for example, exploration, locomotor activity, or cognitive processes, as these systems are potentially confounding factors when assessing anxiety (Ohl, 2005; van der Staay, 2006). The reliable detection, using appropriate diagnostic criteria, of behaviour indicative of anxiety is the prerequisite to allow for the identification of pathological anxiety, i.e. anxiety lacking adaptive value.

6. Behavioural expression of anxiety

6.1. Avoidance behaviour

Independent from the test set up, there are species-specific behavioural expressions that are indicative of anxiety. For example, it is well known from field studies and laboratory observations that rodents tend to avoid the unprotected area of a novel environment when first entering it (Barnett, 1963; Belzung and Le Pape, 1994; Treit and Fundytus, 1988). Under experimental conditions, rodents will typically start to explore the environment along the walls while avoiding the open, i.e. unprotected, areas (Eilam and Golani, 1989, 1990; van der Staay et al., 1990). Other than this rodent-specific behaviour, most animals will avoid (or very carefully approach) novel and unknown areas, objects, and individuals. The expression of avoidance behaviour depends on physical characteristics, such as the visual capabilities of the animal and will further be influenced by other behavioural systems, such as locomotor activity, motivational factors, and also by the animals' exploration strategy.

"*Exploration is evoked by novel stimuli and consists of behavioural acts and postures that permit the collection of information about new objects and unfamiliar parts of the environment*" (Crusio, 2001), and is essential to adapt behaviourally due to growing experiences. To be able to do so, an animal must overcome its initial avoidance-induced behavioural inhibition (McNaughton and Gray, 2000). If full inhibition is maintained, it will finally disable the individual to obtain information about the environment. This has to be noticed as a non-adaptive expression of avoidance behaviour, probably mirroring pathological anxiety.

6.2. Exploration vs. inhibition

Being confronted with novelty, behaviour in animals is determined by the conflict between the drive to explore the unknown environment, object, or animal (including humans) on the one side, and the motivation to avoid potential danger on the other. The exploratory behaviour may comprise a broad spectrum of different behavioural patterns such as risk assessment behaviours (stretched body postures), walking, sniffing, and manipulating objects (Barnett, 1963; Kelley, 1993; Shelden, 1968). Exploration can be partially or completely inhibited by anxiety (see above), therefore reduced exploration might represent an indirect measure of anxiety (Crawley and Goodwin, 1980; Handley and Mithani, 1984; Pellow et al., 1985). This inhibition of exploratory behaviour can be reversed by treatment with anxiolytic compounds (Belzung and Berton, 1997; Griebel et al., 1993; Rodgers et al., 1992).

When analysing anxiety-related behaviour in animals it must be taken into account that primary alterations in exploratory motivation can affect measures of anxiety (Belzung, 1999), Notably, pathological anxiety can only be diagnosed if exploratory motivation is present and which then is inadequately inhibited by avoidance behaviour (see Fig. 1).

6.3. Collection of information: risk assessment

When confronted with an unknown or threatening situation, animals display species-specific behavioural patterns, such as stretched body postures and directed sniffing in rats and mice, which are categorised as risk assessment behaviour (Blanchard and Blanchard, 1989; Cruz et al., 1994; Rodgers et al., 1997). The biological function of these behaviours is to gather information regarding the potential threat by cautiously approaching the potentially threatening stimuli and by scanning the surroundings (e.g., to find hiding opportunities or flight routes). Risk assessment behaviour is thought to be a defensive behaviour (Blanchard et al., 1993) and is indicative of anxiety (see Fig. 2).

It is of note that ethological measures indicate that risk assessment behaviour represents a behavioural system independent from avoidance behaviour (Cruz et al., 1994; Ohl et al., 2001c; Rodgers and Johnson, 1995). These

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behavioural patterns of risk assessment appear to be more sensitive than standard measures of avoidance behaviour (Rodgers and Cole, 1994; Shepherd et al., 1994). This might be due to the fact that risk assessment behaviours are still displayed when the animal has already overcome its avoidance of, for example, a novel object. Under pathological conditions, risk assessment behaviour may be the only expression of exploratory motivation, representing a potentially highly useful diagnostic instrument.

6.4. Coping styles

In response to unpleasant emotions (due to, for example, experience of punishment or non-reward, or induced by unfamiliarity with novel situations and stimuli; see Fig. 1, upper part) evolutionarily primitive subcortical circuits are activated. The amygdala and its projection areas are part of these circuits (see also Rosen and Schulkin, 1998; Sullivan et al., 1999; Charney and Drevets, 2002). Their activation evokes specific autonomic and behavioural responses (such as changes in heart rate, and fight or flight responses; see Table 1 and Fig. 2). Evolutionarily, these responses prepare the animal to cope with dangers (Lang et al., 2000).

Individuals differ in their styles of coping with environmental demands and challenges. Koolhaas et al. (1999) distinguish two coping styles, or stress response patterns: proactive (or active) coping, and reactive coping. Proactive coping is characterized by an intrinsically driven, rigid response (e.g. aggression), whereas reactive coping is characterized by responses that are triggered by the environment. The reactive coping style is believed to be more flexible and adaptive (Campbell et al., 2003). Depending on the individuals' coping style, the expression of pathological anxiety may drastically differ. Still, it is unknown whether the occurrence of hyper-aggression as a symptom of pathological anxiety depends on the respective coping style of the individual.

6.5. Cognitive processes – a driving force behind anxiety?

Unfortunately, both cognition and anxiety are highly complex, multi-faceted phenomena (Clement and Chapouthier, 1998), and their interaction still is matter of research. In humans, anxiety disorders are characterized by 'worries' (DSM-IV, 1994), unwanted disturbing thoughts, and information processing abnormalities (McNally, 1998) that are difficult or impossible to measure directly in animals. A fundamental relationship between anxiety and cognitive processes has been demonstrated (Beuzen and Belzung, 1995; McNaughton, 1997). It has been argued that cognitive alterations may be the primary presenting feature of pathological anxiety (Hindmarch, 1998). Gray (1990) suggested that anxiety emerges when there is a mismatch between the information perceived by an individual and the information already stored. McNaughton (1997) hypothesized that generalized anxiety disorder could be the consequence of a cognitive dysfunction which results in inappropriate emotional responses. On the other hand there is ample evidence that emotional arousal modulates affective memory and declarative memory (i.e. factual knowledge) for emotional events (Cahill and McGaugh, 1998; McGaugh et al., 1996), in particular through stronger negative associations with the (perceived) anxiety-inducing aversive stimuli. This in turn may further increase the level of anxiety (McNaughton, 1997). Anxiety thus may derive from false alarms in the absence of factual danger or threat.

Conditioning processes may increase the subject's sensitivity to interoceptive and exteroceptive cues (Battaglia and Ogliari, 2005), triggered by the exaggerated anticipation or perception of threats, which is incommensurate with the actual situation (see our definition). However, it has recently been shown that this is not an inevitable process: extremes in anxiety-related behaviour in rats can affect cognitive performance in a highly adaptive manner (Ohl et al., 2002, 2003). Pathological anxiety, in contrast, by definition severely compromises an individual's adaptive capabilities and thus interferes with adequate responses in the anxiety eliciting situation.

The strategy to adapt to or cope with the anxiety inducing situation is strongly dependant on cognitive processing since external and internal stimuli (such as increased arousal) must be compared with previously stored experiences, i.e. memories of past anxiety situations and reactions (Ingram and Kendall, 1987; see also Fig. 1). Based on this evaluation, the animal responds behaviourally.

7. Relevance of scientific evidence

7.1. Pet animals

It has been reported that behavioural problems in pets often lead to relinquishment (Salman et al., 1998) or even euthanasia (Overall, 2005). In dogs, for example, separation anxiety, which frequently occurs together with hyper-aggression, destructive behaviour, inappropriate defecation and urination, excessive barking, whining, and hyperactivity, is one of the most common reasons to consult animal behavioural specialists (Appleby and Pluijmakers, 2003; King et al., 2000). Notably, the phenomenon of pet separation anxiety is not limited to dogs and has also been described for cats (Schwartz, 2003).

Although separation anxiety is clinically described as a behavioural disorder and, thus a pathological variant of anxiety (Overall, 2000), the causal aetiology of this phenomenon is still a matter of intensive research (Appleby and Pluijmakers, 2003; Overall, 2000). This is mainly due to the fact that the diagnosis is largely depending on: (1) owners' reports, and (2) integrated concepts combining the behavioural syndrome and (neuro) physiological processes are still under development, although insight is growing fast (e.g. Chatherall, 2003; Lang et al., 2000; McNaughton and Corr, 2004).

7.2. Farm animals

There is growing public attention on the impact of emotional disturbances in farm animals that potentially jeopardise welfare. Behavioural dysfunctions such as "extreme" anxiety in farm animals are typically recognized when productivity is affected or when handling of the animal becomes difficult or impossible. The reasons for this behavioural abnormality remain largely unknown. It has, for example, been shown that repeated early isolation in domestic piglets can lead to long-lasting changes in physiology and behaviour, reducing adaptive capabilities in later life (Kanitz et al., 2004). In poultry, potential strategies to handle "hysteria in laying hens" – a condition that may reflect pathological anxiety – by treatment (Laycock and Bal, 1990) or genetic selection programmes (Muir and Craig, 1998) are being developed.

7.3. Laboratory animals

In laboratory animals, dysfunctions in emotional behaviour not only compromise their welfare, but may also fundamentally affect physiological functioning and, as a consequence, may impact on experimental results even in non-behavioural studies (McEwen, 2003). Such effects are likely to reduce dramatically the reliability of the study results, thus ultimately leading to an increasing number of experimental animals to be used. Moreover, specific demands in terms of housing and treatment can be hypothesized for animals differing emotionally.

The emotional phenotype of laboratory animals is however rarely taken into account when designing animal experiments or defining housing standards. There are a number of reasons for this, including: (1) the emotional phenotype is not yet known; (2) the effects of the emotional phenotype on behaviour and non-behavioural measures are not sufficiently appreciated or, even worse, neglected; (3) due to our ignorance about anxiety-inducing features of environments, we unintentionally create housing and testing conditions that exceed the animals' adaptive capabilities.

8. Conclusions

Independent of the animal species or group, the systematic scientific investigation of the behavioural expression and underlying mechanisms of pathological anxiety is a prerequisite for reliably diagnosing and distinguishing it from "normal" anxiety. In the field of laboratory animal sciences, concern about, and attention for, the danger of undetected but disturbing effects (e.g. false negative or positive results) of pathological anxiety on behavioural and non-behavioural measures is growing (Ohl, 2005; McEwen, 2003). Also, with respect to pet and farm animal sciences, the possible influence of pathological anxiety on observable behaviour, but also on the health status and welfare, deserves more attention.

A broader awareness of the problem and the need for better diagnostic tools has consequences in two areas. Firstly, and in the short term, "treatment" of the afflicted animals, for example by specialized training programmes (e.g. Appleby and Pluijmakers, 2003), may ameliorate the pathological anxiety and may help affected individuals to cope adequately with their environment, in particular in social interactions with other animals and humans. The therapeutic intervention may consist of treating the anxiety, identifying its sources and removing them, or of addressing both (Lang et al., 2000). Secondly, in the long run, breeding programs must ban animals displaying pathological anxiety from reproduction, to eliminate this phenotype from the breed (e.g. Muir and Craig, 1998).

In order to advance and steer this process, the description of the behavioural profile should be an integral part of the breed standard, listing both the desired and the undesired behavioural characteristics of a breed. In farm animals, one may assume that "pathological anxiety" hardly exists, because this trait severely interferes with productivity, extremely complicates handling of these animals, and thus is under severe selection pressure in breeding programs. Where it occurs, however, it deserves the breeders' full attention and actions to eliminate the phenotype through appropriate breeding schedules.

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