Stress and Pheromonatherapy in Small Animal Clinical Behaviour

Daniel Mills, Maya Braem Dube and Helen Zulch

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Preface

This book is the culmination of many years of research and experience, and we are grateful to colleagues, friends and students (too many to mention) who have helped us develop our ideas on these topics over this time. We appreciate your generosity, openness and constructive criticism in equal measure. Science makes progress through discussion, sharing and a willingness to change ideas as new knowledge and opinion becomes available; and it is in this spirit that we have written this text. We have tried to address several emerging issues within the field of clinical animal behaviour, some more controversial than others. But this controversy makes them academically interesting, since at times we have to resort to the basic principles of biology and scientific philosophy to make a judgement about what we consider to be the most appropriate interpretation of what we perceive. It is fair to say that differences of opinion have been a feature of pheromonatherapy from the outset, ever since Patrick Pageat appeared on the world stage at the World Small Animal Veterinary Association (WSAVA) in 1996 and suggested that the facial secretions of the cat consisted of five pheromone fractions, one of which appeared to inhibit urine spraying.

For some, there was concern over the use of the term 'pheromone' in this context, especially when it became apparent that the fraction was in fact a mixture of chemicals rather than a single substance, since this did not fit with the common view of a pheromone. Another issue was that this mixture seemed to consist of relatively common fatty acids. How could these have such powerful effects? Pheromones were largely considered to be specific chemicals that triggered the release of behaviour (recent work shows that ants can use some of these chemicals in a much more flexible way than was previously appreciated, but their role in mammals, who have more flexible behaviour patterns, is more questionable), although a possible exception related to sexual attractants and chemicals that caused sexual arousal in males (what some might call our 'base urges' – reflecting a highly cultural perspective on behavioural control). So what was this French vet doing using the term 'pheromone' in relation to chemicals which seemed to have broader effects on behaviour? Some suggested the term 'social odour' or simply 'semiochemical' should be used instead. However, as we will argue later, this perhaps ignores some of these chemicals' special properties relating to the control of emotional processes, and we should not be distracted by semantics, but instead focus on the claims being made.

The inclusion of *Valeriana* extract in the early commercial formulations raised further concerns among sceptics: they suggested that the fatty acid element was just a placebo and that the effect (if there was one) was due to the

psychoactive properties of this herbal extract. However, this herbal fraction has only ever been included in the commercial sprays and never the diffusers, which have been shown to have a similar level of efficacy. The use of this fraction for the management of spraying was also recently subjected to the most rigorous form of assessment in medical treatment evaluation (meta-analysis) and found to be significantly better than placebo, but even so sceptics remain. Healthy scepticism is good for science, but evangelical preaching of opinion against scientific evidence, like blind acceptance, is not. We hope this book will help the reader to distinguish between these extremes and contribute to the debate on either side in a more informed way. What is important is that we make rational and consistent judgments when faced with uncertainty and are prepared to change our opinion as new evidence comes to light. Otherwise it is a matter of faith, not science.

The use of feline facial and other supposed 'pheromone' fractions extracted from a wider range of anatomical sites and species in the control of behaviour has also been quite an alien concept to many within the veterinary profession (who were the original target of the marketing of these products). So it is not surprising that there has been much confusion and some misunderstanding. It is perhaps for this reason that Ceva Animal Health, the commercial producer of the main products currently available, has invested in a sustained programme of research into their application and use, seeing education as key to acceptance. This includes a lot of research by the first author of this text, much of which was directly supported by Ceva, but only ever with a view to obtaining independent opinion and evaluation. Unlike some of the horror reports which are heard about in the human medical field, Ceva has never sought a spin on our interpretation of results. Rather, it has sought to learn alongside us, and it is fair to say our opinions have changed over time. Also, as data have accumulated and our understanding has increased, the use of pheromonatherapy has been more broadly embraced by both the veterinary profession and nonveterinary behaviourists alike. However, much remains to be learned about their specific mechanism of action, and so this text is a starting point.

In the beginning, many vets were also unclear about how relevant this emerging field of clinical animal behaviour was to them. We hope, as guardians of animal welfare, with a special legal obligation in many countries to this effect, that it is now much clearer, despite the fact that at the time of writing, in the UK, only the treatment of behaviour problems with drugs is considered to be a veterinary act subject to any specific legal regulation. All other aspects of treatment are subject to no such regulation, although attempts are being made to develop benchmark standards for the recognition of professional competence by the Animal Behaviour and Training Council (www.abtcouncil.org.uk).

It is not just the veterinary profession that has been confused. Even within the broader field of clinical behaviour practitioners there is no widely accepted paradigm for the discipline, with some advocating a more medical approach, akin to that used in human psychiatry, and others emphasising the importance of psychology and ethology to the understanding of these problems. Our approach is unashamedly broadly biological, since it is this which underpins

all life sciences. However, even within this academic field there remains much debate on many relevant topics, including the regulation of behaviour. Animal behaviorism, in an effort to reduce subjective bias, has focused on the observable – stimuli and responses – with what happens between these being largely ignored or avoided for fear of being unscientific. As a result, the importance of normal affective systems (emotional reactions, moods and temperament) in regulating behaviour has perhaps not been fully appreciated, and it has lacked much consistency in its application in practice. It is our contention that a deeper understanding of these affective systems is what distinguishes a behaviour counsellor from an animal trainer. Our focus is on creating a happy and well-behaved animal, rather than simply an obedient one. Fitting in with others involves adjusting one's behaviour in anticipation of events, rather than just attending to cues for instruction.

A lot has happened in the last 15 years or so to address many of the issues mentioned in this introduction, which is why we feel this book is timely. It represents a synthesis of ideas, offering not only a framework for understanding how pheromonatherapy can be used to encourage desirable behaviour (when there is still much to learn) but also a fresh approach to understanding the nature of clinical animal behaviour problems. This, we believe, allows for more precise treatment and a deeper understanding, especially of those cases that do not seem to fit the typical presentation. Science is by its very nature imperfect, since it progresses by falsifying what we previously believed to be true, but that does not mean we should be afraid to propose ideas to explain our observations. While we have tried to develop our ideas logically on the basis of sound science, we have also tried to produce a readily accessible text for those who want to learn more about the subject. Over time, we hope to produce more academic publications expanding on the details of some of the underpinning concepts presented here; but for now we wish to present an initial framework, which we believe will help to move things on, since it allows us to generate testable hypotheses.

We do not want arguments over the meaning of words to get in the way of the overall message, nor do we want to invent a totally new language. Instead, and especially with a view to a readership beyond the academic, we have tried to accept 'the diversity of language' as a starting point. In order to do this, we feel it is important to define how *we* are using certain terms, in order to try to avoid confusion. In time it may be that a new language is necessary, but we will leave that for another day. Thus we continue to use the word 'pheromone' in places where some might prefer 'semiochemical', 'social odour' or some other term, largely out of recognition that 'pheromonatherapy' appears to have entered the English language as a word used to describe the deliberate application of these chemicals to affect the behaviour of captive animals. But in using the word 'pheromone' thus, we think it is important to highlight at the outset that the reader should be careful about making assumptions as to how the clinically used chemicals work or exactly what can be generalised on the basis of our knowledge of pheromones in a broader academic setting.

At many points in the book, we try to clarify other potential inconsistencies in scientific language in a similar way. Indeed, we also devote a considerable amount

of text to the other keyword in the title of this volume: 'stress'. We argue that the concept is of very limited value without an appreciation of its qualitative property in a given context if we wish to manage it effectively. The limitations of previous thinking only become more fully appreciated in light of an understanding of the role of affective systems in the control of behaviour, a topic which has often been ignored, but which we also try to address at some length in Part I. Although Part I deals with some fundamental concepts, it only focuses on those areas which are likely to be less familiar to the typical reader. It does not deal with those which we believe are well covered in other clinical animal behaviour texts, such as pure and applied learning theory, history-taking and counselling skills, so the less experienced reader should reference such other texts as appropriate.

In Part II we illustrate the application of these concepts to a range of specific situations. This is not intended to be an exhaustive list of common conditions encountered, or even of those in which pheromonatherapy may be applied, but rather covers those situations in which there has been the most research to support pheromonatherapy's efficacy. Thus we do not deal with aggressive behaviour, despite its obvious prevalence in clinical-behaviour case loads. The research is not finished and clearly no trial is definitive, but we try to explain why we favour a particular interpretation of the uncertainty that remains. Recently, Ceva Animal Health has produced a freely available text summarising each published trial to date. We have therefore not repeated the details here; rather, the reader can obtain this supplementary text from Ceva if interested.

In conclusion, it is our genuine hope that this book will be useful to both academics and practitioners alike in the field of clinical animal behaviour and will stimulate further positive and constructive debate, not just about the use of pheromonatherapy but also about other important concepts relevant to animal welfare. We do not wish you to blindly believe everything, nor do we want you to dismiss things out of hand, but rather we hope to make you think and reflect, and perhaps to make new discoveries as a consequence. It is in this way that we can genuinely hope to do all that is in our power for the ultimate benefit of our patients.

PART I

Principles and Concepts Underpinning the Management of Stress-related Behaviour Problems

Chapter 1

How Animals Respond to Change

1.1 UNDERPINNING PRINCIPLES RELATING TO STRESS IN COMPANION ANIMALS

1.1.1 *STRESS AND CHANGE*

It has been said that the only constant in life is change, and it seems that some of us cope better with this than others. In this chapter we will explore why this might be. We will focus on factors that not only affect humans but are also relevant to nonhuman animals. Attempting to adapt to change is an intrinsic part of being alive. As a feature of any living system, the environment changes around us all the time, and we have a number of mechanisms for dealing with this. Two obvious ones that are commonly described in the literature are:

- *Physiological processes*: Pure changes in physiology are often thought of as being relatively simple (metabolic changes), for example a change in sweating when the body's temperature starts to rise. These changes may be mediated by either the nervous or the endocrine system, or a combination of both. Often changes in simple physiology are relatively inexpensive, energetically speaking, for an animal to implement.
- *Behavioural processes*: Behaviour responses, for example an animal panting when it is hot (Figure 1.1), involve much greater use of resources and energy, and so are perhaps better considered as the second line of response in the majority of cases. However, physiological processes are at the root of changes in behaviour too: it is just that behaviour changes are more obvious and involve a shift in the animal's posture or position.

Sometimes an animal adapts to a stressor by making a mental adjustment (cognitive change), for example accepting something novel in the environment as nonthreatening, and this too is ultimately a reflection of physiological changes in the brain, even though we might focus on the cognitive outcome.

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Fig. 1.1 Panting is a response to thermal stress. Animals encounter stressors all the time, but their behavioural flexibility means they can usually cope without significant distress.

Thus, in response to stress, we can recognise three types of change in the body:

- A metabolic shift.
- A change in behaviour.
- A psychological adjustment.

These are not independent, but rather are usually closely related, though perhaps with one being more obvious than another at a given time, depending on the demands being made or anticipated given the circumstances. Overt changes in behaviour are typically more demanding and are therefore often a secondary line of defence when metabolic shifts are not possible or do not work.

1.1.2 *HOMEOSTASIS AND ALLOSTASIS*

The concept of homeostasis has dominated thinking about how animals adapt to change for a long time, but in its purest form it has the potential to limit our understanding in some important ways, as we will see. *Homeostasis* basically means that an animal's body works to restore an optimal state whenever this is disturbed (stressed). So if blood sugar goes up, the body will try to bring it down again, since high blood sugar can be harmful. An immediate response might be to increase production of insulin in order to increase the uptake of glucose by cells in the body. At a behavioural level, an animal may stop feeding in these circumstances, and at a cognitive level it may no longer show positive interest in cues suggesting food. The concept of homeostasis can be applied not only to stressors associated with internal changes, such as changes in blood sugar, but also to external changes such as unpleasant and dangerous environments or situations that are confusing to the animal: thus, if something scares the animal it may run away in order to restore the preferred state of relaxation in a safe and secure environment. Sometimes an animal must work very hard to restore balance, or it

Fig. 1.2 A dog trying to escape from its kennel. Successful escape would restore homeostasis, but this is not possible because of the height of the pen walls. It is better to see the walls as a barrier which gives rise to frustration to the animal's attempts at escape than to simply consider the animal bored, since this focuses attention on the types of intervention which might be most effective. If we consider the animal to be bored, we are using a vague concept and our recommendations for intervention may be equally vague – such as unspecified 'environmental enrichment'. As we will see later in the text, if we recognise that the animal is frustrated by a specific stimulus, we can ask the question: what action is being frustrated and why? The answer in this case is that there are things outside it wants to gain access to. So treatment should focus on not only removing this frustrated desire by ensuring the stimuli outside are less interesting, but also, and more importantly, making the inside more engaging for the animal. This means enrichment needs to be applied that is dynamic and interesting. A few toys will not be enough.

may be frustrated in its efforts by an inescapable situation, such as when a dog wants to get out of a kennel (Figure 1.2).

From these examples, it should be apparent that although responses may share some common features, such as an increase in arousal, stress responses vary according to the nature of the trigger. Thus the specific response is quite different when the trigger is a rise in blood sugar than when it is frustration at a barrier.

The key feature of homeostasis that we will now consider more closely is that the body tries to minimise the impact of stressors (things that disturb us from an optimal set point in some way) by *responding* to changes. The word 'responding' is emphasised as it suggests that it is the disturbance which drives the process.

A concern with this idea is that if we provide an animal with a balanced diet, fresh water, an optimal temperature and so on in a nonthreatening environment, we might be tempted to think that the animal should not be stressed. This was one of the errors which led to the belief that factory farming would be good for animals. We now recognise that because animals have evolved in environments in which change inevitably exists, their bodies have come to expect change and so they are driven to do things even when everything seems optimal. This is probably because such a state is never very long-lasting in nature, so there is no evolved mechanism to simply accept that life is good and will remain as such.

An outcome of the evolutionary expectation that life exists within an ever-changing environment is the development of an anticipation of change within the core processes governing the regulation of the body's metabolism. The body therefore changes in anticipation of change. This is what is meant by the term *allostasis*, which provides a better model than homeostasis for many physiological processes. The key difference between allostasis and homeostasis is that in allostasis responses are driven by the *anticipation of change* as well as by actual change. So if an animal is always fed at the same time each day, insulin will eventually be produced at a certain time, even if there is no food available and even if this leads to a significant lowering of blood sugar which the animal then has to counter by producing the antagonistic (opposing) hormone glucagon.

From the preceding example, it might be tempting to think of allostasis as simply a training of the homeostatic response, but it is much more than that, as it helps to explain why animals have natural rhythms to their metabolism and activity even in the absence of cues. It also helps us to understand the wider and changeable psychological needs of animals, which we discuss in the next section.

1.1.3 *PSYCHOLOGICAL NEEDS*

One of the things which many animals do when they have all their fundamental physiological needs met is seek information. There are several reasons why this is useful if there is an inbuilt expectation of change. For example, it allows them potentially to exploit resources more effectively in future (e.g. by knowing where the next meal could come from if the current supply were to dry up) and it might reduce the risk of future harm (e.g. by knowing how strong different potential competitors are). Therefore, when times are good we will often see animals investigate and play much more. Object play allows animals to learn about the physical properties of things, while social play can help them learn about the characteristics of other individuals, including their strengths and weaknesses. An important implication of this is that, in such circumstances, providing for some of these activities should not be considered a luxury, but rather essential for an animal's well-being. In humans, a hierarchy of needs has been described in the literature by Maslow (1943), which indicates what individuals seek as different needs are met. While some of the higher levels originally described may not be directly applicable to nonhuman animals, this hierarchy can be adapted to give a guide as to animals' priorities in different circumstances (Figure 1.3).

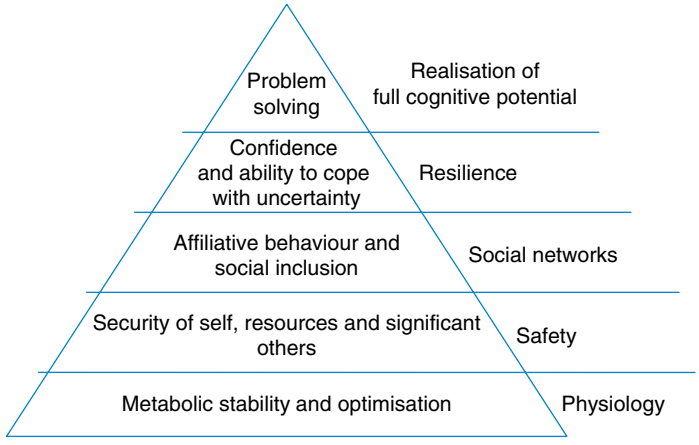

Fig. 1.3 A hierarchy of needs for animals, adapted from Maslow's hierarchy of needs for humans. The labels to the right indicate the type of need, with those at the bottom being initially most important. As the lower-level needs are increasingly met, the higher-level needs become increasingly important. Thus if an animal's physiological needs are being met, the need for safety and security is more pressing, so it can be expected that the animal will become less willing to take high risks to obtain its food and so on. All of the needs depend on the acquisition of information in order to be met efficiently, but the type of information changes with ascending levels.

Another use of this hierarchy is to help us appreciate why an animal is not performing particularly well in a given aspect of its life and what needs to be done to help resolve the issue. For example, an owner might complain that their pet lacks confidence, and this might be at least partly due to unstable social relationships at home, which mean that the animal is focusing resources on social networks as a priority. Without addressing this lower-level need, it may be difficult for the animal to grow in confidence, as its priorities are elsewhere.

This hierarchy indicates that safety or a sense of safety is a big priority for animals after their physiological needs have been met. Most pets are well fed and watered, and so the issue of safety deserves further consideration. *Safety* broadly means knowing that you can escape potential harm, and so requires that the animal has some freedom to withdraw from situations that it finds unpleasant. In the home, this means the animal has a safe haven, or some other secure attachment. We will return frequently to the importance of providing coping strategies when we discuss the use of pheromones in a clinical context to help animals cope in a variety of settings. The need for safety also helps us to understand why the inappropriate use of punishment, especially by an owner, can be so disruptive to an animal's well-being. Quite apart from being ineffective in altering the underlying motivation for the unwanted behavioural response and disrupting the bond between the owner and their pet, the inconsistent use of aversive methods leads to the animal's lacking a sense of safety. Thus common basic requirements for managing almost any behaviour problem are that all punishment should cease and that a healthy relationship between the owner and

their pet should be established. Only with these foundations in place can we expect the animal to have the confidence to change inappropriate emotional responses. Once again, pheromones can be useful in this process, as we shall see. However, there are also important constraints on what can be achieved, which are considered in the next section.

1.1.4 *THE GENOME LAG AND EVOLUTIONARY CONSTRAINTS*

Companion animals evolved in a particular environment over centuries and today often live in a very different one. The modern environment can be very stressful for both humans and their companion animals. The fact that evolution may not have equipped them with the mechanisms to deal with the sorts of stress or that they face in the domestic home can pose a problem. Let us look at the dog as an example: it is a social animal and is adapted to live in close social groups. Hence, being left alone can be very stressful for a dog and it will use the mechanisms that it has received through evolution to cope with this situation, such as howling in order to try to reestablish contact with the members of its group. Other possible behaviours it might attempt include trying to escape from the environment in which it is isolated, which can result in considerable property damage (Figure 1.4). We might think that a dog should know it can't break through a wall, but solid, all-enclosing walls are not something it has evolved to deal with. An important thing to appreciate here is that although a behaviour may not be very effective (i.e. maladaptive), that does not mean the underlying behavioural control

Fig. 1.4 A dog may try to escape even if it cannot succeed. The lack of success can simply lead to persistent behaviour, as seen in the damage to this door.

systems are broken (i.e. malfunctional). There is sometimes a tendency to think that a behaviour must be pathological if it does not bring an obvious benefit, but this is not always the case; an animal may simply be using its evolutionary rules of thumb in an inappropriate context because of the artificiality of the environment. This has important implications as it means we should not be looking for treatments to correct a supposed malfunction, but rather we should be looking at the environmental contingencies and perceptions of the animal that are leading it to perform in this way. However, although the response may be a functional one, that is not to say it cannot be problematic or give rise to pathological processes as a result of its inappropriate deployment in given circumstances (we will return to this in Section 1.2).

Most stress responses have evolved in order to help animals cope with acute (short-term) crises, for example 'There is a predator and I need to escape', 'I am alone and I need my friends' and so on. Unfortunately, the stresses that we tend to face in modern living are often much more prolonged (possibly going on for years), and even a mild stress can end up having quite an impact, as an animal's coping mechanisms are not developed to deal with prolonged challenge. By way of example, imagine you are required to hold up a cup of water. It is not a big problem and you should be able to do it easily. But if you have to hold it up for hours it becomes a much more significant issue. In the same way, the odd stressor may be fine on its own, but when it goes on for months or years we can see wider effects on the functioning of an animal and the system it lives in. We will return to this later when we talk about factors affecting the impact of a stressor. At this point it is simply important to appreciate that animals are often not well adapted to deal with stressors that go on for a long time, even if they are small, because in nature stressors are typically resolved quite quickly one way or another. This is one reason why a thorough history of any animal presented for problem behaviour is important. For example, two cats may have never got on very well together but have tolerated each other. Over time this can lead to more substantial changes such as certain recurring health problems, an increased risk of diabetes and perhaps more overt aggressive behaviour problems.

Another important evolutionary constraint on adaptation relates to the type of response elicited. Different species have evolved in different niches and have different lifestyles. Accordingly, they may use different rules of thumb to resolve an issue. Thus cats and dogs differ in the typical behaviours that they can offer in order to help them adapt:

- Dogs are a social species that use a well-developed communication system to cooperate and to coordinate their behaviour with other group members.
- Cats are more independent but are generally capable of living in groups. Their social communication skills are not so refined, as living alone is their evolutionary inheritance given the type of prey they feed upon, which does not require pack hunting.

Thus a dog, when faced with a problem, will be much more likely to look for social support for help (which might involve trying to engage the owner in the issue) than a cat, which would be more likely to try to resolve things itself. In either case,

this can involve the animal changing the chemical environment around itself in order to cope. Alarm pheromones can help an animal avoid a dangerous area and so remain safe, but there are also pheromones that signal safety, which allow the animal to focus less energy on environmental monitoring and more on other things. We will discuss these pheromones in detail later, but first we need to consider the concept of safety in more detail.

1.1.5 *SAFETY AND ITS ROLE IN LIFE*

We have already mentioned that safety is an important need for animals, but it is worth considering in more detail what it means to be safe and the consequences of this.

A safe place is somewhere that is associated with the absence of harm and the absence of signs of harm. It is therefore a place in which an animal can relax and explore with confidence. This has many important implications for animal management and welfare. A *safe haven* is somewhere that an animal feels in control of events. One of the most common misunderstandings that we encounter is confusion between a 'safe haven' and a 'bolt hole'. A *bolt hole* is somewhere that an animal runs to in order to hide or to watch and hope that whatever is bothering it will pass. A *safe haven* is somewhere that an animal goes where it feels safe and in control of events. It is quite difficult to convert a bolt hole into a safe haven; to create a safe haven we need to create a place where the animal is not disturbed and where it can choose to go if it does not want to interact with us. If we really want to give the pet a place where it is truly in control, we must not impose ourselves or our interests on it in this area. It is obviously important for all who come into contact with the animal to appreciate and respect this.

Young animals frequently use an attachment figure (typically the mother) as a secure base from which to explore the world. This can be transferred to other individuals, but such individuals must be supportive of the animal, recognising and respecting its communication and responding appropriately (e.g. not forcing it into situations with which it expresses discomfort). Pheromones, like dog-appeasing pheromone (DAP), which is produced by bitches shortly after whelping, appear to be particularly important in this process. As we will see later, these chemicals seem to have an intrinsically reassuring effect through the limbic system, which helps provide the pup with a secure base from which to explore and learn about the world.

As a simple rule, it is important for social individuals to have at least two points of safety in their lives:

- A physical place (safe haven).
- A social companion (secure base).

The importance of a social companion may be lower for a more independent individual, but recent work suggests that this should not be generalised to species; that is, while cats in the wild may be quite independent, in the home they can form strong attachments and dependencies. If an animal has no need for a social companion, the physical safe haven may be especially important.

1.1.6 *STRESSORS AND THE STRESS RESPONSE*

The term 'stress' is often used in a very confusing way to refer to both an animal's response to something and the cause of that response. In this book, we will use the term *stress response* to describe an animal's behavioural and physiological reactions to a threat and the term *stressor* to describe the trigger of these: that is, the stimulus.

The *stress response* can be defined as the physiological, behavioural and psychological response to a challenge to an individual's optimal state of well-being. As we have already seen, this is not a simply defined fixed point, as might be thought from a homeostatic perspective, but will vary with numerous factors. When trying to assess the stress response, it is important to distinguish the measures we can assess objectively from our interpretation of them. For example, a dog may run away in response to a loud noise, which is something we can measure objectively (e.g. the time it takes to respond (*latency*), its speed, the distance it travels, changes in its heart rate). But if we say 'The dog is scared', that is an interpretation, which may be much more difficult to quantify and objectify. There is room for debate when it comes to interpretations; for example, some dogs that run up to their owner when they hear a loud noise are not actually scared but are just seeking the owner's attention or have found that the noise is a good way of getting the owner to give them more attention – this has been referred to as a *pseudofear*. In these cases it is important to examine what the owner does in response to the pet coming up to them and to determine whether they function as the previously mentioned secure base or whether they are reinforcing the dog's attention-seeking behaviour, as these outcomes will require different types of intervention to resolve. Owners will typically report interpretations and one of our jobs as clinicians is to sensitively and objectively assess these, rather than accept them as fact.

If we consider a *stressor* as anything which moves an animal out of its normal optimal range, this means there are many different types of stressor and that not all stressors are bad. It further means that there are likely to be many forms of *stress response*, as different responses are required to cope with different types of stressor. An animal can be moved out of its normal optimal range by something unpleasant: for example, a pet running away from a loud noise or a cat hiding from a chasing dog. Both of these responses lead to increased arousal. On the other hand, increased arousal is also required for essential activities like reproduction and play that are generally considered to be more pleasurable. Hence, we should be careful not to interpret all stressors or the resulting changes elicited as indisputable evidence of poor welfare. The determination of an animal's well-being is an inference which should be drawn from multiple pieces of evidence (a process sometimes referred to as *triangulation*).

There are many features which relate to a stressor's impact on an individual, such as:

- *The type and number of stressors*: Some animals may find auditory stressors, such as the level of noise, more stressful than visual ones. Similarly, if certain stressors are combined, this may be much more stressful for some individuals and not for others. For example, in the case of fireworks, some animals are

able to cope with the noise or with a flash of light on its own, but when the noise and the visual stressor occur simultaneously, the animal perceives the situation as much more threatening.

- *The intensity of the stressor*: Some animals may be able to cope with softer noises, for example, but find it difficult when the volume increases beyond a certain level.
- *The duration of the stressor*: As already discussed, a stressor might be quite mild, but if it goes on for a long period of time it can be difficult for an animal to cope with it. It is therefore important to evaluate how long a particular stressful situation has been going on.
- *The predictability of the stressor*: The concept of predictability can be very important for an animal's welfare. If something is very predictable, it can make it easier for the animal to prepare its defences and to cope as a result. For example, an animal might habituate to certain stressors that have been going on for a long time (e.g. road work in front of the house) but react strongly to rarely and unpredictably occurring stressors (e.g. a thunderstorm). If the animal cannot predict the situation, it cannot divert resources in order to cope, as it does not know when the problem is going to arise. For a given individual, the optimal level of predictability of a stressor varies enormously: something that is too predictable can actually also be stressful, as we do seek some change in our environment. We often interpret it as 'boring' if something is extremely predictable. We know it is going to happen and so we do not pay much attention to it. If something that the animal knows it can't cope with is predictable, this increases arousal in advance without an expectation of being able to cope.
- *The level of control an animal has over a stressor*: If an animal has control over its environment, it is easier for it to cope and to take appropriate measures. If we return to the example of sound sensitivities, things like fireworks and thunderstorms are often very difficult for an animal, because it has very little control over when the sound will happen (in this example, predictability and control are linked, but this is not always the case). This is made worse if it has no safe haven. Noises like thunderstorms can be particularly problematic, because the sound seems to move around in an uncontrollable way and cannot be clearly located – the stressor is both unpredictable and uncontrollable. Having no way of removing itself from the situation because it is locked in the house and/or being on its own may be additional stressors that an animal has to cope with at such times. Hence, it is not surprising that problems such as noise fears and separation distress often occur together. When a case is referred for one of these conditions, it is very important to check that the other is not present as well, as they may be linked.
- *The previous consequences of the potential stressor – what the animal learns*: Has the animal been able to cope in the past? If it has then even quite severe situations may be tolerated. But if an animal has had other unpleasant experiences associated with a potential stressor, something that might seem relatively mild to us may actually become very severe for it. For example, if a dog starts to show mild signs of anxiety in response to a noise and the owner tells it off, the mild noise now becomes a predictor of punishment from the owner and so can actually

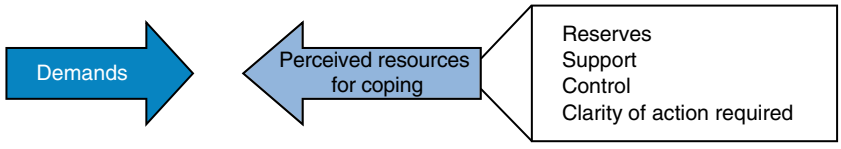

Fig. 1.5 Stressors give rise to concern over an animal's welfare when the demands they impose exceed the animal's perceived resources for coping. There are therefore many features outside the properties of the stressor which affect its potential impact. Resources for coping include not only the physical reserves of the animal but also aspects which are often influenced by the handler, such as the level of perceived support the animal has, the level of perceived control the animal has over the situation and the clarity of action required to deal with the problem. The fact that this process depends on a perception of the animal's means there are few hard and fast rules about whether a given stressor is necessarily harmful to a given individual.

become much more stressful, and the animal is likely to react even more strongly the next time it faces the stressor or predictors of the stressor.

When we think about the impact of a stressor, we often tend to focus on its physical properties, such as its intensity, duration, frequency, predictability and so on, but as the last few examples show, a central principle underpinning how much impact a stressor will have relates to the animal's interpretation of whether and how it can cope (Figure 1.5). An animal may face quite a big challenge, but if it predicts (and has learned) it can cope with change (i.e. it is resilient), the impact of the stressor may be rather small, including that on the animal's welfare. On the other hand, a phobic animal may not be able to cope with a relatively minor and – to bystanders – obviously harmless stressor, such as a fly. Coping with it seems like an insurmountable challenge and the animal's welfare is therefore seriously impacted.

1.1.7 *SELYE AND THE GENERAL ADAPTATION SYNDROME*

By now it should be apparent that stress responses are quite varied; nonetheless, there is still a tendency to refer to a general stress response. This idea is particularly associated with Hans Selye (1907–1982) and what he termed the *General Adaptation Syndrome (GAS)*. This basically describes the most common form of arousal, resulting from a range of stressors. It describes three phases of response to a stressor and has greatly influenced our understanding of how stress can be harmful to the body, and so deserves some attention.

Selye's three phases of the GAS consist of:

- *The alarm phase*: Selye termed the immediate response the *alarm phase* or the *alarm reaction*, with the following reactions within the body:
  - *An increase in both epinephrine (adrenaline) and norepinephrine (noradrenaline)*: These are hormones from the centre of the adrenal gland, the *adrenal medulla*,

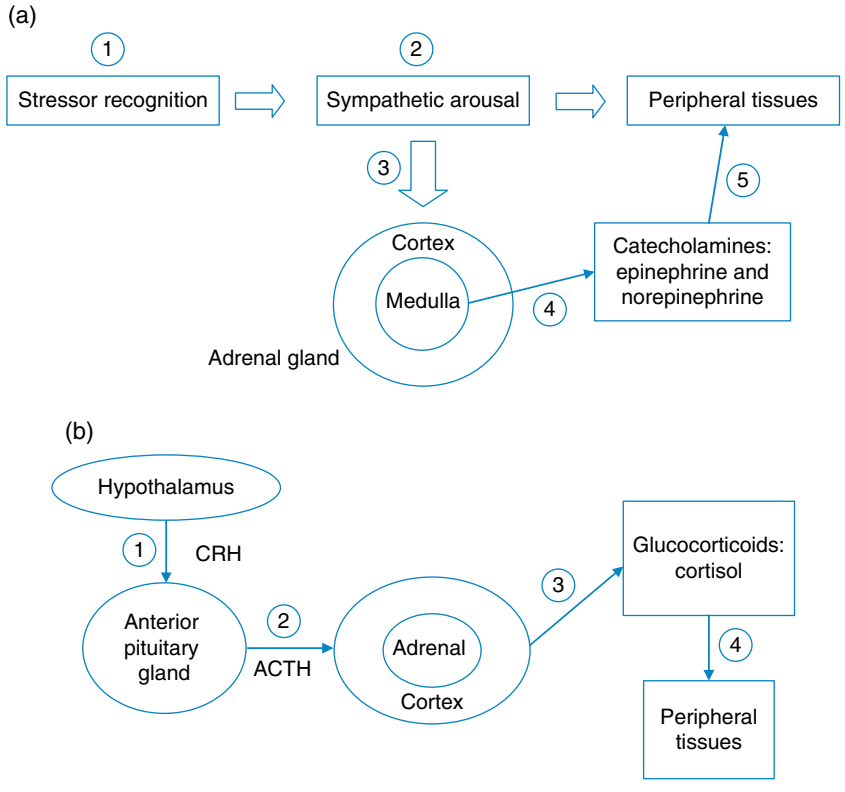

Fig. 1.6 Schematic of the sympathetico-adrenal (a) and hypothalamic–pituitary–adrenal (b) axes and general physiological and behavioural changes. (a) (1) the stressor is recognised, which leads to (2) changes in the sympathetic nervous system, which is the fight/flight system; (3) nerves associated with the sympathetic nervous system travel to the core of the adrenal: the medulla; (4) the medulla releases epinephrine and norepinephrine, otherwise known as *catecholamines*; (5) the nervous system also directly impacts on specific tissues – both the catecholamines and the direct nervous input result in a variety of changes in these peripheral tissues, which prepare them for action. (b) (1) the impact of a potential stressor is registered within the hypothalamus of the brain, which results in a release of *corticotrophin releasing hormone* (CRH); (2) CRH is transported to the anterior pituitary gland, which sits at the base of the brain and results in the release of *adrenocorticotrophic hormone* (ACTH), another releasing hormone that affects the adrenal cortex – this response requires a cascade of hormones in order to take effect and so is a slower response than that from the adrenal medulla; (3) this cascade of hormones results in the release of glucocorticoids, which include the hormone *cortisol*; (4) the glucocorticoids in turn have a variety of effects on peripheral tissues.

which are released as a result of increased activity in the sympathetic nervous system (Figure 1.6). Their production is closely associated with the fight, flight, freeze and fidget (or fiddling about/flirting) strategies, which are aimed at repelling, running away from, cautiously tolerating and redirecting attention away from the stressor, respectively.

- *An increase in corticosteroids (the hormones cortisol or corticosterone, depending on the species) from the cortex of the adrenal gland*: This is a result of activation of the hypothalamic–pituitary–adrenal (HPA) axis (Figure 1.6).
- *An increase in blood sugar*: Epinephrine, norepinephrine and corticosteroids all raise blood sugar and so help mobilise energy reserves. Another hormone change that we see in this immediate reaction is a drop in hormones such as insulin, whose role is to lower blood glucose. So, overall there is a rise in blood glucose in anticipation of having to take action, such as running away from a predator or a serious threat.
- *Diversion of reserves within the body to support immediate survival*: The body diverts its reserves towards taking immediate action in response to the potential threat and away from longer-term activities. So, in the alarm phase, the hormone changes also result in a suppression of the immune system and a reduction of the hormones that help increase productivity. Obviously, if you are faced with a predator, functions like reproduction and fighting off disease are relatively unimportant compared to staying alive in the immediate future. There is no point being very healthy but dead!

- *The period of resistance*: After the immediate alarm phase, Selye described what he termed a *period of resistance*, which has the following characteristics:
  - The levels of adrenal hormones (epinephrine, norepinephrine, corticosteroids) all remain quite high.
  - The levels of the *anabolics* (i.e. molecules that help build up reserves in the body, such as the blood glucose-lowering hormone insulin) return back to normal.
  - Raised blood glucose levels are maintained, in order to sustain and prepare for further activity as might be necessary.
- *Adaptation or exhaustion phase*: It may be that the previously mentioned response is sufficient for the animal to be able to cope, in which case the animal *adapts* successfully. However, if the response persists for a long period of time, *exhaustion* may occur, with a risk of a whole range of pathological processes as a result. It is important to appreciate that the balance between adaptation and exhaustion can be a fine one and that animals may appear to adapt for a reasonable period of time but ultimately become exhausted, which can lead to serious health and welfare problems (consider the example of holding up the cup of water). Even if an animal appears to be adapting, it may be making an enormous effort to do so and that too is a cause for concern.

Although Selye proposed that the GAS was the general way in which animals responded to stressful situations, it was soon recognised that it was not perhaps quite as general as he initially thought. There is a whole range of specific responses that animals may employ when faced with unpleasant situations. For example, many species respond to a rise in the environmental temperature with a drop in corticosteroid levels, rather than an increase. Similarly, when sheep are dehydrated, there may be no perceptible adrenal response at all. This makes sense from an adaptive biological perspective, because raising blood glucose when you are hyperthermic or dehydrated will actually tend to increase activity within the

body and so increase demand for water, as well as raise body temperature further as a result – not to mention that the water may be more useful in aiding cooling through panting or sweating. It makes a lot of sense not to produce a response which is likely to make matters worse.

Animals vary enormously in how they cope with a given stressor, not just between species but also between individuals of the same species. For example, an increase in temperature may be far more difficult for one animal to cope with than another (consider the short-nosed – *brachycephalic* – breeds of dog in this context, which can have difficulty panting efficiently). If we think about changes in the social environment, we will also see enormous individual differences, with some animals showing behavioural problems and others seeming to cope fine.

Another concern over the common interpretation of the GAS is the emphasis it puts on *cortisol*. It is easy to see why this happens as there seems to be an ever-growing list of known effects of cortisol on the body. Not only does it have the physiological effects discussed, it also produces behavioural changes and biases. For example, as part of its effect in helping to maintain blood sugar, it actually stimulates appetite. This is why you might feel the need to eat lots of chocolate when you are chronically stressed. This may seem strange, considering that we would expect an animal's priority to be escape, but it is important to note that we are now talking about longer-term stressors. The role of cortisol in this context is to help the animal cope with these longer-term impacts of stress; for example, after the stress is over, the raised cortisol will stimulate the animal to eat and, thereby, to replenish its reserves – this helps to explain why physiological arousal lasts longer than the stimulus causing it (a characteristic of emotional reactions). Cortisol also produces quite important cognitive changes. It biases an animal's attention towards negative events, which means that the animal may view otherwise neutral stimuli as potentially threatening. This is not just of academic interest, but also of clinical importance, because in clinical practice synthetic and much more powerful versions of the glucocorticoids are used to control a whole range of medical conditions. One must keep in mind that treating an animal with these medical drugs may actually induce concerning changes in the animal's behaviour as a result. An increase in appetite is a commonly recognised side effect of the use of glucocorticoids, but less attention has been paid to their cognitive effects, and so some behavioural advice – aimed at reducing the impact of an increased sensitivity to aversive events – may be useful when dispensing these drugs.

Prolonged or excessive cortisol can be quite toxic to parts of the brain involved in memory, like the hippocampus, with obvious and immediately apparent effects. For example, as a result of chronic exposure an animal may forget things that it has previously learned. In the human literature, *stress-induced dishabituation*, which is when a person forgets things that they have previously learned as a result of chronic stress, is well documented, and we are increasingly recognising it in companion animals too. This can result in the appearance of a number of behavioural problems, including noise fears. If a problem appears at an unusual age, it is important to check whether or not the animal appears to have been under chronic stress recently, particularly if the behaviour in question is one which the animal had learned not to show: this might be a strong indicator of stress-induced

dishabituation. In such cases, the focus of treatment must be not just to correct the behaviour problem but to look at general stress management for the animal so that the problem goes and stays away.

We may also see changes in the reactivity of the adrenal cortex, particularly in the case of long-term or repeated stimulation. These changes, however, can be difficult to predict, as the adrenal cortex may become less responsive or exhausted, or it may become sensitised. This is clearly an area in need of further research. The relatively routine *ACTH stimulation test* can be useful in some cases when we see a marked change, in the sense of either an over- or an underreaction, in the adrenal response. Changes in response can indicate that an animal has been subject to long-term stress, but the fact that individuals vary enormously in their normal response to the test often makes interpretation difficult. The test would really be most useful if we could assay an animal before it underwent a stressful experience as well as after, in order to assess the stressor's impact. If we were to perform the test before an owner moved house and again afterwards, we might see marked changes in the responsiveness. We mention this here simply because it is something that we might want to make better use of in future.

Undoubtedly cortisol is very important, but it is just one of many hormones which are involved in how animals cope with environmental changes (i.e. stressors in the environment). Cortisol is produced as a result of ACTH release from the anterior part of the pituitary gland in the brain. This structure also produces a whole range of reproductively important hormones: notably *prolactin* (Prl), most widely known for its role in milk production in females, but with other effects not associated with reproduction; and *luteinising hormone* (LH) and *follicle stimulating hormone* (FSH), which occur in both males and females and are associated with the production of the gametes. All of these hormones rise after initial stress and can stay elevated for several hours after the stress has disappeared. However, in response to chronic stress, levels will fall, and so we may see knock-on effects of stress with respect to reproduction.

Prolactin is of particular and growing interest within the field of veterinary behavioural medicine in that it is regulated by inhibition rather than stimulation. The removal of inhibition results in its release. Dopamine, a neurotransmitter generally involved in the activation of goal-directedness of a wide range of behaviours, seems to be one of the main factors that inhibits the release of prolactin. A high release of prolactin suggests that there is very little dopamine coming from the hypothalamus to control it; that is, the animal is not seeking out the good things in life. This may explain a whole range of behavioural changes that can be seen in relation to stress. Dopamine is associated with behavioural activation; that is, the approach an animal takes towards potential signs of reward or potential rewards. If an animal has low levels of dopamine, it may become more apathetic and less responsive towards rewards, which is reflected in its behaviours. It makes sense that an animal becomes less sensitive to rewards in times of stress, because it is probably focusing on escaping from an unpleasant situation.

In France there has been an effort to try to validate a system for both scoring and monitoring animals' responses to chronic stress, which has resulted in the production of the *Evaluation of a Dog's Emotional Disorder (EDED)* scale (see Appendix A).

Interestingly, recent work has suggested that the scoring used in this system might correlate quite well with prolactin levels.

The relationship between dopamine and prolactin and our ability to indirectly infer the level of dopamine activity from prolactin screening might also have implications for the choice of drugs used to treat particular disorders. In treating behaviour problems, it has been noted that not all patients respond in the same manner to the same medication. The postulated explanation for this is the involvement of different neurotransmitters in the same superficial behaviour presentation in different patients. If one can assess which neurotransmitters are involved in a patient's behaviour, a more targeted use of medication can be implemented. For example, if an animal is showing changes in behaviour that seem to be associated with a reduction in dopamine levels, it makes sense to use drugs, such as selegiline, that are likely to act on the dopamine system. In support of this, data are emerging to show that where anxiety is associated with a change in prolactin level, drugs like selegiline may be more effective than drugs like fluoxetine. Fluoxetine might also be indicated for the presenting complaint, but it works on the serotonin neurotransmitter system, indicating that often more than one neurotransmitter system is involved in behaviour and in behavioural changes.

There are a number of other hormonal changes in the pituitary gland that occur in response to stress, particularly changes in *oxytocin*, which is associated with bonding behaviour, and the endogenous *opiates* (*endorphins*, *enkephalins* and *dynorphins*), which are also associated with bonding but in addition also with *analgesia* (pain-killing). Both of these groups of chemicals also have effects on memory that should not be underestimated.

The domestic environment is very complex and individual animals will vary in how they perceive different changes in this environment according not just to genetic differences but also to their developmental history. Developmental history is referred to as *ontogeny* within the scientific literature. Individual differences are very important for a number of reasons. First of all, they remind us that it is actually the animal's perception of the stressor rather than its physical nature that is important. What is too loud for one dog or cat may be fine for another. It is important when working with cases that we appreciate that all animals are individuals. In behaviour therapy, it is particularly important to pay attention to individual differences, because when it comes to finding solutions, they have to be tailored to the individual animal, its circumstances and the resources of the system in which it lives. We should avoid the temptation of thinking one solution fits all.

Finally, contrary to its common representation, the GAS is not very specific to unpleasant situations. In fact, the changes in cortisol seem to be a reaction to any change that requires increased arousal, whether it is pleasurable or aversive. Based on this, some people have proposed using two different terms to distinguish between stressful situations that are harmful and those that are not:

- *Distress*: Responses associated with unpleasant events, such as punishment or fear.
- *Eustress*: Stressful situations which an animal may find pleasurable, such as reproduction or play. *Eu* is the Greek word for 'well'.