



## Behavioural changes in dogs treated with corticosteroids



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### HIGHLIGHTS

- We aimed to identify behavioural changes in dogs treated with corticosteroids.
- Dogs on corticosteroids showed behaviour associated with a negative affective state.
- In a behavioural test, dogs on corticosteroids avoided a mildly aversive stimulus.
- Dog owners should be advised by veterinarians about behavioural risk management.

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### ABSTRACT

In human medicine, psychiatric side effects among patients on corticosteroid therapy are widely reported, but this appears to have been largely overlooked in the animal literature despite glucocorticoids being widely used in veterinary medicine. Therefore the aim of the current study was to identify possible psycho-behavioural changes in dogs treated with corticosteroids. Two different methodologies were used. Firstly, dog owners were asked to fill a 12 item questionnaire aimed at further validating the initial results of a previous survey relating to changes seen when their dog was receiving corticosteroid treatment. In a second study, a population of dogs undertook behavioural tests aimed at objectively identifying changes when receiving corticosteroid therapy.

In the first study, a sample of owners whose dogs were receiving treatment for dermatological, orthopaedic or other conditions evaluated their dogs' behaviour on and off therapy, using a seven point scale. The survey was completed by 44 dog owners with dogs receiving treatment with a range of corticosteroid preparations (mainly prednisolone and methylprednisolone) and 54 dog owners with dogs receiving treatment with other drugs, mainly antibiotics and non-steroidal anti-inflammatory drugs. Dogs under corticosteroid treatment were reported to be significantly less playful, more nervous/restless, more fearful/less confident, more aggressive in the presence of food, more prone to barking, more prone to startle, more prone to reacting aggressively when disturbed, and more prone to avoiding people or unusual situations.

In the second study, eleven "treatment" dogs were tested both before and during corticosteroid treatment with either methyl-prednisolone or prednisolone to assess their sensitivity to a potentially aversive sound stimulus. Eleven control dogs were also tested at the same time intervals in the same environment. Dogs were exposed to a brief dog growl while they explored bowls containing food and their behaviour was video recorded. Treatment dogs were found to investigate the area in the vicinity of the bowls for significantly less time and to eat significantly fewer pieces of food when on corticosteroids, compared to control dogs, after hearing the growl. These results provide the first empirical evidence of possible adverse psycho-behavioural side effects in a veterinary clinical setting following the use of corticosteroids, and suggest the need for concomitant behavioural advice when these drugs are used in general veterinary practise to avoid the risks associated with these changes.

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### 1. Introduction

Glucocorticoids are widely used in veterinary practice but are also among the most important mediators of the stress-response [1,2]. This response has physiological, behavioural, cognitive and

emotional components, having the potential to inhibit positively motivated responses and to increase anxiety-related behaviours [3–5]. Glucocorticoids mediate changes in cognition, learning and emotional processes through the activation of glucocorticoid receptors in diverse brain areas from the prefrontal cortex through to the hippocampus, basal ganglia and amygdala [3]. Both excesses and deficits in glucocorticoid can lead to impairment of learned and emotional processes and responses [6].

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The therapeutic use of glucocorticoid drugs in companion animals is associated with several well recognized physical side effects including gastro-intestinal problems, suppression of adrenal gland function and increased risk of infections [7,8]; possible psychological side effects have not received much attention beyond a preliminary survey reported by the authors [9]. However, in human medicine, several surveys and case reports have shown that important psychiatric side effects can occur in patients on corticosteroid therapy. It has been suggested that the onset of corticosteroid-induced psychiatric disturbances might be linked to pre-existing individual psychological characteristics such as personality, with these reactions reflecting an extreme version of a patient's usual stress reaction [10–12]. Increasing attention is being given to these effects in human patients, receiving long term treatment [11,13,14]. Neurological toxicity due to the drug itself or the synergistic action of drugs administered concurrently have been postulated for the unexpected behavioural and psychiatric effects of these medications when prescribed for physical diseases [5], these effects are probably most often related to the neurochemical cascades linked to the stress response [14–16].

Alongside studies in human medicine, there is abundant evidence of the influence of exogenous pituitary adrenal hormones on animal behaviour but not specifically in a therapeutic context as might occur in companion animals. Studies in laboratory animals have shown that exogenous glucocorticoids can affect cognitive functions such as learning and memory [6,17–19]. An effect on the emotional states of animals has also been hypothesized with, for example, the experimental administration of corticosteroids to rats appearing to influence their subsequent emotional response to unexpected reductions in reward size [20]. This study showed that rats treated with corticosteroids responded to an unexpected downshift in reward magnitude by showing a significantly greater decrease in their consummatory behaviour – interpreted as an expression of their emotional response – compared to a control group subjected to the same procedure. Many of the behavioural effects of corticosteroids would be expected if these chemicals induced a negative cognitive bias, e.g. a greater sensitivity to potentially threatening stimuli in the environment [21].

Investigating the potential negative behavioural side effects of glucocorticoid drugs in companion animals is clearly important in order to make a full risk–benefit analysis concerning their use, and to ensure that appropriate advice can be given to owners and veterinarians when these drugs are prescribed. Therefore the present study aimed to investigate the effects of corticosteroid therapies on dog behaviour:

firstly, through a retrospective study using questionnaire responses concerning the behaviour of dogs when on and off corticosteroid therapy; and secondly, through a case–control study of the responses of subjects in a behavioural test aimed at assessing the animal's response to a potentially threatening sound stimulus.

## 2. Materials and methods

### 2.1. Questionnaire study

A 12 item questionnaire was completed by dog owners with dogs receiving or having recently received drug treatment, preferably for dermatological or orthopaedic conditions. The questionnaire was informed by the results of a previous survey [9]. Seven of the 12 items were selected on the basis of the results of a previous survey [9], with five further questions ('fillers') relating to other behavioural changes not identified in the previous survey selected among behaviours that frequently cause complaints by dog owners [22,23], but not thought to be influenced by corticosteroids. These were inserted partly as 'fillers' and to aid validation of target effects [24]. The questionnaire was published via the Internet in both English and Italian, with a paper version also distributed to Italian veterinary clinic clients. Questionnaires were back translated by independent mother tongue translators to assess the consistency of the two versions. The items were scored on a seven point scale with two scores for each question posed: one score for the respondent's perception when the animal was receiving pharmacological treatment for the condition and one for when the animal was not receiving pharmacological treatment (Fig. 1).

The introductory part of the questionnaire gathered demographic data relating to both the owner and their dog, information about the drugs being given to the dog at the time of survey (such as type of drug, time of administration and doses) and information about the type of condition/disease for which it was being used. The respondents were asked to mention all drugs taken in the same period for the same or other concomitant conditions. The questionnaire was to be completed on the Internet and advertised through veterinary associations, pet websites and magazines both in Italy and UK. Paper questionnaires were also distributed in veterinary clinics in the north of Italy.

Questions are illustrated in Table 1 and Items 1 (Play behaviour), 5 (Attention seeking), 7 (Obedience), 8 (Guarding behaviour) and 12 (Mounting behaviour) were added as additional fillers.

WHEN YOU ANSWER THE FOLLOWING QUESTIONS, YOU ARE KINDLY REQUESTED TO THINK, AT FIRST, ABOUT THE BEHAVIOUR OF YOUR DOG BEFORE STARTING THE DRUG AND PUT AN X WHERE APPROPRIATE IN THE UPPER UNSHADED STRIP. THEN YOU SHOULD THINK ABOUT YOUR DOG'S BEHAVIOUR WHILE YOUR DOG IS TAKING THE DRUG AND PUT AN X WHERE APPROPRIATE IN THE DARKER, LOWER STRIP

**Q1. Play behaviour.** Some dogs are very motivated to play with people, other dogs or toys. On a scale from 1 to 7 where 1 is 'not very playful' and 7 is 'very playful' how would you rate your dog's behaviour?

Not very playful ←————→ Very playful

Without drug							
With drug							
	1	2	3	4	5	6	7

Fig. 1. Example of question and scoring system used in owner questionnaire: Q1 Play Behaviour.

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