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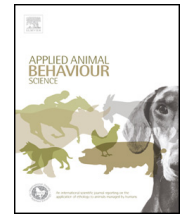
Effectiveness of fluoxetine to control fur-chewing behaviour in the chinchilla (*Chinchilla lanigera*)

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ABSTRACT

Due to its complexity and the relative lack of scientific reports, fur-chewing may be considered as one of the most challenging behavioural problems common to captive chinchillas. The development of this behaviour in commercial farms and the increasing popularity of this species as a pet have increased the public demands for a treatment. The objective of this work was to evaluate the effectiveness of fluoxetine to control the development of chinchillas' fur-chewing behaviour, using an oral dose of 10 mg/kg/day for a 90 days treatment period. For the measurement of the fur-chewing affected area and its variation during treatment as external sign of whether or not the behaviour was controlled, digital pictures were taken at 0, 45, 75 and 90 days of treatment and after drug withdrawal at 140 days. Results indicated that the greatest difference in percentages of body area affected by the behaviour in control vs. treated animals was observed after 75 days of treatment. However, this was not due to a decrease in the amount of body area affected by fur-chewing in treated animals, but conversely to an increase in the symptoms observed in control animals, that showed a ~10% increase in the fur-chewing affected body area than at the beginning of the experiments. Only ~46% of the fluoxetine treated animals showed a significant reduction in the body area affected by fur-chewing. In summary, the use of fluoxetine in fur-chewing chinchillas showed limited success, mostly reducing the progression of the behaviour.

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1. Introduction

Through many generations, the chinchilla has been domesticated and bred because it bears one of the most valuable pelts in the world. However, the establishment of intensive captive breeding programmes led to the description of an abnormal repetitive behaviour known as "fur-chewing" (Ponzio et al., 2007). Fur-chewers repetitively chew their own fur about half-way down the length of the hair, either constantly or at intervals, sometimes regrowing it completely in between (Rancher's Handbook, 1987); the behaviour resembles an exaggerated form of grooming in which the fur is chewed rather than simply groomed (Ponzio et al., 2007) and the most affected areas include flanks and sides and usually appear darker due to underfur exposure. Fur-chewing can range from slight (only a few tufts of hair are chewed) to very severe (all the fur in regions of the body that the animal can reach is chewed) (Ponzio et al., 2007, 2012).

The aetiology of the behaviour has caused endless discussions over the years and available reports presented little evidence, relying predominantly on anecdotes and 'expert opinions'. In recent years, with the acknowledgement of abnormal repetitive behaviours commonly displayed by many species in zoo, farm, and laboratory environments (Mason and Latham, 2004; Mason, 2006), the hypothesis that fur-chewing is a type of compulsive/impulsive behaviour and that stress plays a role in its development and performance has arisen. Few scientific

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works were published about this animal condition and the underlying causation of fur-chewing behaviour is still being investigated and debated (Jenkins, 1992; Mösslacher, 1986; Ponzio et al., 2007, 2012; Tisljar et al., 2002).

In general, these kinds of goal-directed repetitive abnormal behaviours where the fur/feathers are self-removed have been linked to the human obsessive-compulsive disorder (OCD) (Garner et al., 2004; Mon-Fanelli et al., 1999) and trichotillomania (Bordnick et al., 1994; Garner et al., 2004; Stein et al., 1994) in terms of phenomenology and aetiology (e.g. barbering in mice, psychogenic alopecia in cats, feather picking in birds, etc.).

The use of psychotropic medications has become increasingly more common in veterinary medicine and combined with behavioural and environmental modifications, they made the treatment of various repetitive disorders more successful (Simpson and Simpson, 1996). Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), is one of the most commonly used treatments (Crowell-Davis and Murray, 2006). As a consequence, there is more information about safety, side effects, and efficacy in various species for this medication than any other (Crowell-Davis and Murray, 2006).

Direct comparison of the effects of fluoxetine on repetitive behaviours is difficult due to differences in categorization of abnormal behaviour between studies (e.g. stereotypies vs. impulsive/compulsive behaviours). However, they share enough characteristics in order for research to be mutually relevant and the known serotonin involvement in OCD warrants studies on its role in other abnormal repetitive behaviours (Meers and Ödberg, 2005). It should also be born in mind that the same drug can have opposite effects in different individuals, even if the pathology is developed under seemingly similar conditions (Meers and Ödberg, 2005).

Although information on the underlying motivational basis of chinchilla fur-chewing is currently ambiguous or unavailable for a full treatment approach (including also behavioural and environmental modifications), the development of this behaviour in commercial farms and the increasing popularity of this species as pet have increased the public demands for a treatment. Therefore, the main objective of this work was to evaluate the effectiveness of fluoxetine to control the development of chinchillas' fur-chewing behaviour. An additional objective was to develop a more reliable and proper scoring method to assess treatment efficacy.

2. Materials and methods

2.1. Animals and housing

A total of 34, sexually mature domestic chinchillas (Chinchilla lanigera) were used in this study, showing a slight or severe condition of fur-chewing behaviour (Ponzio et al., 2007). Animals were individually housed in a commercial chinchilla farm in Córdoba, Argentina, in individual stainless steel cages (W: 32 cm, H: 30 cm, L: 50 cm) with wood shavings as a substrate, exposed to natural fluctuations in photoperiod (spring and summer: 14.2 and 14.0 h of light, respectively; 31°S–64°W) and controlled temperature (20–25 °C). Pelleted chinchilla food (Chinworld, Buenos Aires, Argentina) and water were provided ad libitum, and a cube of compressed alfalfa was fed once weekly. A spoon of marble powder was added to the substrate of each cage on a regular basis in order for the animals to be able to dustbathe, to keep the fur dry and uncompressed. Animals were randomly assigned to two experimental groups and subjected to control (eight males and eleven females; 33.1 ± 2.8 months old) or treatment conditions (six males and nine females; 29.8 ± 2.05 months old). Within each group, animals were further classified according to the amount of body area affected by fur-chewing using a visual severity score, as slight (only a few tufts of hair are chewed) or severe (one or both sides of the body or hips are chewed) (Ponzio et al., 2007, 2012).

All experiments were conducted in accordance with the National Institutes of Health, Guide for the Care and Use of Laboratory Animals.

2.2. Pharmacological treatment and administration

Based on the dosages employed in other rodents (rats, mice) and those used to treat similar conditions in other species (cat, dog, parrot, horse) (Crowell-Davis and Murray, 2006), a dose of 10 mg/kg/day of fluoxetine was selected for the chinchillas.

Due to the bitter taste of the substance and to ensure full consumption of the daily dose, the pure drug (fluoxetine, Laboratorios Gador S.A., Buenos Aires, Argentina) was mixed with corn syrup (Kero[TM], Unilever Food Solutions, Buenos Aires, Argentina) and then injected inside a raisin with a syringe in the amount of an individual dose. Untreated raisins were administered to the control group. All raisins were also covered with a powder vitamin supplement normally used by the breeders (Vionate S, Novartis Argentina S.A, Buenos Aires, Argentina) and freshly prepared every week.

Animals were fed with the drug filled raisins (treatment) or with regular raisins but also covered with the vitamin supplement (control) every morning for 90 consecutive days, which coincides with the time required for a chinchilla fur follicle to re-grow completely. Subsequently, a gradual drug removal regime was applied to the treated group for 3 consecutive weeks using decreasing doses of 7.5, 5.0 and 2.5 mg/kg/day (days 90–110). Observations made by the keepers corroborated that the animals completely consumed the raisins containing the drug. The control animals were also fed with raisins without the drug for the 3 additional weeks.

2.3. Treatment evaluations

For the measurement of the body area affected by fur-chewing and the variation during treatment in both groups (as an external sign of whether or not the behaviour was modified), digital pictures were taken at 0, 45, 75 and 90 days of treatment and after drug withdrawal at 140 days after experiment onset. On each occasion, animals were briefly removed from their home cages, held by the tail and suspended in the air face down. Pictures of both body sides were then taken (Fig. 1).
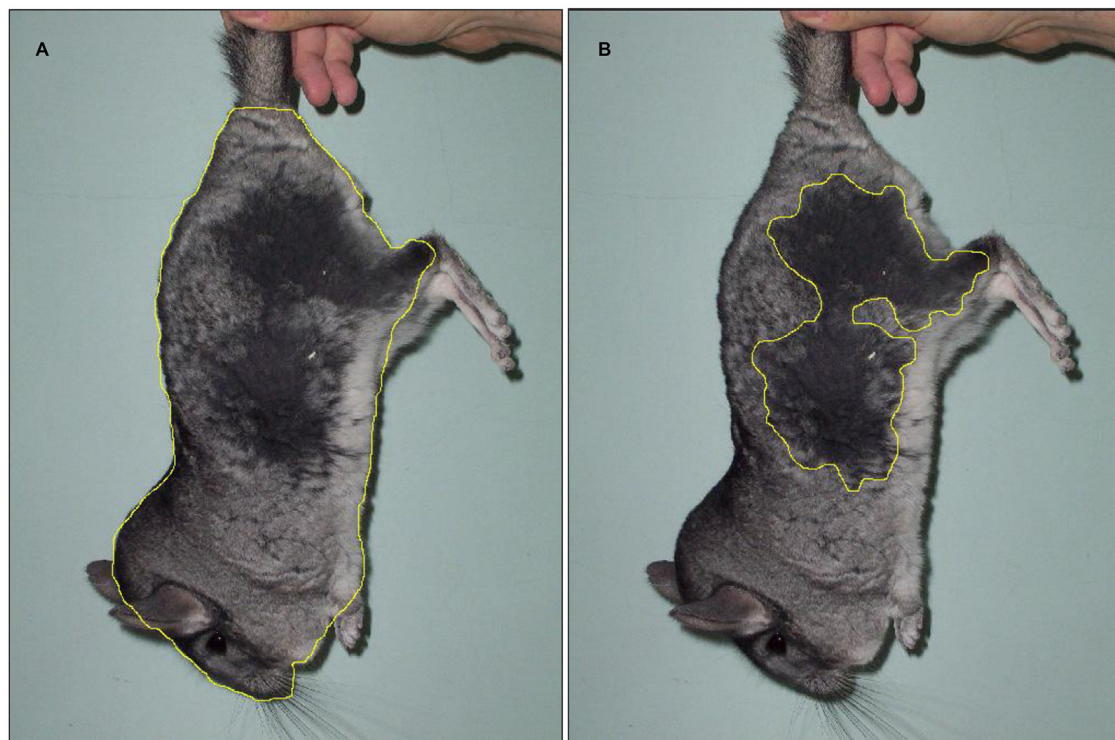
Fig. 1. Procedure used for the measurement of the body area showing signs of the fur-chewing behaviour in a chinchilla. A technician used the freehand selection tool to measure the total body area (with the exception of the tail; panel A) and the affected area in each body side (panel B).

For the images analysis, the Image J software was used (W. Rasband, Research Services Branch, National Institute of Mental Health, Bethesda, MD, USA). A technician, blind to the treatments, used the freehand selection tool to measure the total head and body area (with the exception of the tail) and the body area affected by fur-chewing on both sides (Fig. 1, panels A and B, respectively); the results were expressed as percentage of the total body area affected by fur-chewing. Because a human degree of error is inherent to this system, each measure was performed three consecutive times and a mean of these values was then used as the final score.

2.4. Statistical analysis

To analyse the precision of our initial scoring system (slight or severe at time 0) we evaluated the body areas affected by fur-chewing in each category using a two-factor (treatment and initial score) linear model followed by the LSD Fisher post hoc test (Table 1). For the analysis of the effect of the drug treatment, a linear mixed effects model for longitudinal data was applied. Treatment, day of evaluation and initial score factors and their interactions were included as the fixed part of the model; meanwhile the animal was included as a random effect term to account for the intra-class correlation of the longitudinal data. The DGC (Di Rienzo, Guzmán and Casanoves) post hoc test was applied to perform the pair-wise comparisons of means (5% significance level) (Di Rienzo et al., 2002). The triple interaction of the factors (drug treatment × day × initial score) was not significant and was not included in the final model. To specifically compare the percentages of animals that

improved, showed no change or increased the performance of the behaviour in both treated and control groups after 75 days of treatment, a Chi-square test was applied to the data. All data were analysed using the Infostat statistical software, version 2012 (Di Rienzo et al., 2012). Numerical routines used to fit the fixed and mixed linear effects models are those implemented in the gls and lme functions respectively. These functions are implemented in the nlme package (Pinheiro et al., 2012) of R (R Core Team, 2012). Residuals of all models were checked for normality and homoscedaticity before analysis.

3. Results

The initial percentages of body area showing signs of the abnormal behaviour (time 0) in control or treated animals are illustrated in Table 1. As expected, animals categorized as slight showed significantly lower percentages of

Table 1
Initial score and percentages of body area affected as consequence of the fur-chewing behaviour in control or fluoxetine treated chinchillas.

Treatment	Initial score	n	% Of body area affected by fur-chewing	Range
Control	Slight	13	7.4 ± 1.9[a]	2.2–13.6
Control	Severe	6	29.3 ± 4.0[b]	13.8–54.1
Fluoxetine	Slight	9	5.42 ± 1.3[a]	2.1–10.0
Fluoxetine	Severe	6	18.4 ± 2.4[b]	13.2–37.0

Data are presented as mean ± SEM. Fluoxetine treatment was 10 mg/kg/day. Control: $n = 8$ males and 11 females; fluoxetine: $n = 6$ males and 9 females. Slight: only a few tufts of hair are chewed; severe: one or both sides of the body or hips are chewed. a vs. b: $P < 0.0001$.
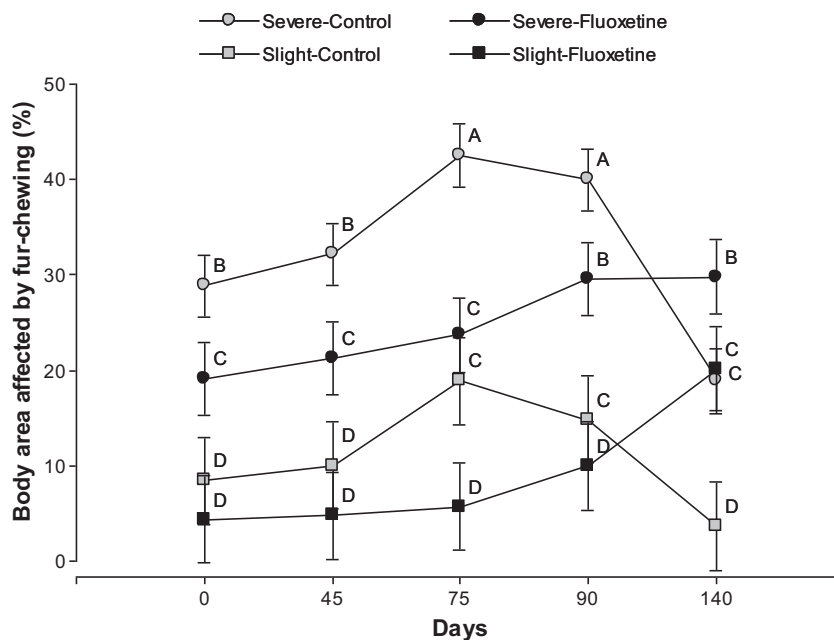
Fig. 2. Percentages of body area showing slight or severe signs of the fur-chewing behaviour in control or fluoxetine treated chinchillas. Animals were treated for 90 days with a dose of 10 mg/kg/day of fluoxetine. A gradual drug removal regime was then applied for 3 consecutive weeks using decreasing doses of 7.5, 5.0 and 2.5 mg/kg/day. Evaluations were performed at 0, 45, 75 and 90 days of treatment and after complete drug withdrawal at 140 days. Slight: only a few tufts of hair are chewed; Severe: one or both sides of the body or hips are chewed. Severe-Control $n = 13$; Severe-Fluoxetine $n = 9$; Slight-Control $n = 6$; Slight-Fluoxetine $n = 6$. Values are represented as mean $\pm$ S.E.M. Different letters denote significant differences at each time point and within groups ($P < 0.05$).

body area affected by fur-chewing (slight vs. severe: $F_{1,119} = 27.3$; $P < 0.0001$) than those categorized as severe using our visual scoring system. The general analysis with the linear mixed effects model showed a significant effect in the interaction drug treatment $\times$ days ($F_{4,119} = 14.31$; $P < 0.0001$).

Before the treatment administration (time 0) a marginal but significant difference was detected in the severely affected animals between the treatment and control groups in the percentage of body area affected by fur-chewing (Fig. 2, drug treatment*initial score: $F_{1,119} = 4.12$; $P = 0.045$). No differences were found at this time in slightly affected animals (control vs. fluoxetine).

Independently of the initial score (slight/severe), fluoxetine treated animals did not show significant reductions in the percentages of body area affected by fur-chewing throughout the treatment period, but continued rather constant. Only 46.6% of the animals under treatment showed a slight improvement (4.2 ± 1.3% reduction in the body area affected by fur-chewing) in the fur condition after 75 days of treatment whereas, on the contrary, most of the control animals showed a clear and significant increase in the occurrence of fur-chewing ($\chi^2 = 7.07$; $P = 0.007$), with 94.7% of the animals showing 13.8 ± 3.4% more of the body area affected (Fig. 2). The rest of the animals in the treated group (53.3%) showed slight signs of an increase in the fur-chewing (9.8 ± 3.2% increase in the body area affected).

Fifty days after the end of the treatment period (day 140), both control groups showed a significant decrease in the percentage of body area affected by fur-chewing and returned nearly to baseline levels ($F_{4,119} = 14.31$; $P < 0.0001$); on the other hand, after complete drug withdrawal, animals with initial slight fur-chewing and treated

with fluoxetine demonstrated a significant increase in the development of the abnormal behaviour ($F_{4,119} = 14.31$; $P < 0.0001$); this effect was not observed in the animals with initial severe fur-chewing and treated with fluoxetine (Fig. 2).

4. Discussion

Due to its complexity and the relative lack of scientific reports, fur-chewing could be considered as one of the most challenging behavioural problems common to captive chinchillas. Therefore and until more information becomes available, this work aimed to test a treatment based on fluoxetine administration. This treatment would result in an increase in serotoninergic neurotransmission, allowing serotonin molecules to act for extended periods of time (Crowell-Davis and Murray, 2006). The onset of the beneficial effects is usually slow and commonly does not occur for 3 to 4 weeks, or even longer (Crowell-Davis and Murray, 2006). Coincidently in our study, the greater difference in percentages of body area affected by fur-chewing between control and treated animals was observed after 75 days (in both groups, slightly or severely affected animals). However, this was not due to the improvement in the fur-chewing condition in treated animals (that stayed rather constant over the experiment), but conversely to an increase in the symptoms observed in control ones, that showed ~10% more of the body area affected by the behaviour than at the onset of the experimental period.

In this respect, there are two key aspects to consider: to our knowledge there are no studies concerning whether fur-chewing in the chinchilla tends to be stable in severity within individual chinchillas, as opposed to varying either

systematically (i.e., with breeding status, ovarian cycle stage, season, or age) or erratically within individuals. The fur-chewing behaviour in both control groups seemed to fluctuate over time with increasing percentages of external signs up to 75 days of observations and a sudden decrease to nearly baseline levels at the end of the experiments (final evaluation time, day 140). Unfortunately, the reasons/explanations for this fluctuation cannot be addressed with the available data. We can only hypothesize that the animals could be additionally affected by the daily disturbance of the keeper during the raisins administration and that a clear effect of fluoxetine was to prevent such an increase. This could be further supported by the fact that fur-chewing suddenly decreased in control animals after the raisins were no longer administered. Indeed, the behaviour has been previously associated with an increased adrenocortical activity and an increased amount of anxiety-like behaviours in the elevated plus-maze test (e.g., decrease in the percentage of entries and time spent in open arms and increase in freezing behaviour), particularly in severe fur-chewing females (Ponzio et al., 2007, 2012; Tisljar et al., 2002; Vanjonack and Johnson, 1973).

On the other hand, only ∼46% of the fluoxetine treated animals showed a clear yet slight improvement in the fur condition. Pharmacological intervention using fluoxetine or other SSRIs have demonstrated different degrees of success when used in other species and related forms of abnormal repetitive behaviours: only 27% of psittacine birds that exhibited phychogenic feather picking (Grindlinger and Ramsay, 1994), 50% of dogs showing acral lick dermatitis (Rapoport et al., 1992; Stein et al., 1992) and ∼50–60% of cats showing psychogenic alopecia (Mertens et al., 2006; Sawyer et al., 1999). Notably, SSRIs are likewise not completely effective in human obsessive compulsive disorder (∼40% of patients do not respond to this treatment), and they are even less effective in trichotillomania (Christenson et al., 1991; Lochner et al., 2005; Streichenwein and Thornby, 1995).

Fifty days after the end of the treatment period, the slight-fluoxetine treated group showed a significant increase in the percentage of body area affected by the behaviour. In this respect, it must be borne in mind that after prolonged administration, it is possible that a down-regulation of serotonin receptors occurs and a rebound effect could be observed (Crowell-Davis and Murray, 2006). This seems to be the case in this study, where although a gradual drug removal regime was applied, a worsening of the symptoms was detected especially in the slightly affected animals.

In veterinary medicine, animals often show resistance to taking medications. This is particularly problematic if it has unpleasant taste and the drug must be given daily for a long period, which is the case of fluoxetine. For animals such as the chinchilla that are fearful and/or susceptible to handling, the difficulties are compounded. The method applied in this work, mixing the drug with a sweetener and providing it inside a raisin, secured the consumption of the entire dose throughout the treatment period.

Finally, proper evaluation of a treatment efficacy requires the use of reliable scoring methods (Van Zeeland et al., 2009). In most studies, behavioural responses are measured by direct observation or video recordings which are subsequently analysed by a researcher that is blind to the treatment. In those cases, each observer must be able to reproduce the scores in repeated tests (within-observer reliability), and different observers must produce scores that both correlate (inter-observer reliability) (Honess et al., 2005). However, because of the active role played by the observer, those methods of behavioural assessment rely on an individuals' perception and judgement, and can therefore be difficult to implement in studies like the present one, where the body area affected by fur-chewing, showed only slight changes overtime. The method we developed in this work, although indirect because it measures the consequences of the behaviour and not its development, provides a more objective and measurable indicator of whether or not the behaviour was controlled by the drug.

5. Conclusion

In summary, the use of fluoxetine in fur-chewing chinchillas showed limited success, mostly reducing the progression of this abnormal repetitive behaviour over time. Further studies should explore the use of higher fluoxetine dosages and probably its use in combination with environmental modification or enrichment.

Conflict of interests

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

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