BEHAVIORAL ASSOCIATIONS WITH FELINE GASTROINTESTINAL AND DERMATOLOGICAL DISORDERS

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Dedication

To Deja, Echo, Albus, Athena, Henry, Sophie, Libby, and many others who inspired me to be curious, kind, and treat every living thing with respect.

> "I hope to make people realize how totally helpless animals are, how dependent on us, trusting as a child must that we will be kind and take care of their needs. They are an obligation put on us, a responsibility we have no right to neglect, nor to violate by cruelty."
>
> - James Herriot

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Abstract

Despite a growing body of evidence that suggests a strong connection between physical and behavioral health in animals, the effects of inflammatory diseases on cat behavior remains understudied. I investigated whether behavior profiles of cats with inflammatory GI and skin diseases differ from those of healthy cats. I also explored whether corticosteroid treatment affected cat behavior. I hypothesized that cats with inflammatory diseases would display more behavioral signs of anxiety than healthy cats and that steroid treatment would correlate with increased anxious behaviors. I identified cats within Penn Vet's patient database that had been diagnosed with inflammatory GI and skin disorders, as well as a control group of healthy cats. The owners completed a feline behavioral assessment survey (Fe-BARQ), and I analyzed the resulting data using the Mann Whitney U test. The results revealed significant behavioral differences between groups. Anxious behaviors were more prevalent in the inflammatory group than the healthy group. The inflammatory group scored higher for purring and trainability than the healthy group. Additionally, cats treated with corticosteroids exhibited more anxious behaviors than healthy and non-steroid treatment groups. This study establishes that cats with inflammatory disorders display more anxious and comfort-soliciting behaviors than healthy cats and that corticosteroid treatment is associated in a higher incidence of anxiety in cats.

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Introduction

The effect of physical disease on the behavior of cats is very pertinent to feline welfare. Physical and behavioral health are closely intertwined, and physical disease has a relevant bearing on the behavior of cats (Merola & Mills 2016). For many animal caretakers, behavioral changes are often the first indication that a problem exists with their pet. Pain, discomfort, and inflammatory diseases are known causes of behavior changes in animals, but studies have shown that clinicians in general practice often dismiss behavioral concerns as being irrelevant to physical disease (Mills et al., 2020). This increases the likelihood that both physical and behavioral disorders go untreated and that the affected animals experience poorer welfare.

A growing body of evidence suggests a strong link between behavioral and physical health. Behavior is generated and regulated by the body, and therefore behavior is connected to all physiological and pathological processes that occur internally (Landsberg et al., 2012). Multiple studies have demonstrated that many behavioral conditions considered to be psychogenic have their roots in physical disease (Horowitz; 1997; Waisglass et al., 2006; Frank, 2014; Camps et al., 2019; Mills et al., 2020). In fact, previous research estimates that up to 80% of dog and cat clinical behavior cases stem from underlying pain and discomfort (Mills et al., 2020).

Just as physical diseases may affect behavior, chronic and acute stress may cause or exacerbate physical symptoms (Berteselli et al., 2005). There is a known

correlation between stress and skin disease and gastrointestinal disorders in humans (Landsberg et al, 2012). Research in dogs and cats has shown that stress initiates and intensifies GI and dermatological diseases, as well as behavioral disorders in both species (Dreschel, 2009; Stella et al., 2011). In cats, chronic stress has been shown to cause a range of sickness behaviors, including gastrointestinal symptoms (vomiting, diarrhea, anorexia) and dermatological symptoms (skin inflammation, overgrooming) (Stella et al., 2011; Stella & Buffington, 2014).

Researchers are increasingly aware of how an animal's microbiome impacts both physical and behavioral health, finding that behavioral changes associated with illness may be a direct result of the microbiota (Collins et al., 2009; Bercik et al., 2011). Stress and anxiety have also been shown to alter gut microbiota in humans, leading to irritable bowel syndrome and inflammatory bowel disease (Bhatia & Tandon, 2005). In dogs and cats, acute fear and chronic anxiety can lead to GI disorders, such as decrease in appetite or anorexia, diarrhea, vomiting or colitis (Landberg et al., 2013).

Because the immune system plays a key role in regulating behavior, it seems likely that inflammatory diseases would affect behavior (Landsberg et al., 2013). Anecdotal evidence from veterinary behaviorists suggests that the most common physical diseases underlying clinical behavior cases are gastrointestinal and dermatological conditions (C. Siracusa, personal communication, 2022).

A review of the current literature revealed that the effects of inflammatory diseases on cat behavior is understudied with marginally more work being done in

other companion species, such as dogs (Horowitz & Mills, 2010; Landsberg et al., 2013; Klinck et al., 2008). To date, few studies have presented definitive evidence showing a correlation between physical discomfort and behavior traits in cats. A number of studies in cats revealed behavioral associations with generalized pain, pain related to elimination, and pain caused by osteoarthritis (Merola & Mills, 2016; Horwitz, 1997; Klinck et al., 2012). A review article described behavioral signs of pain caused by various diseases in cats, including gastrointestinal disease and dermatological disease, and a 2006 study explored medical causes for presumed psychogenic alopecia (Frank, 2014; Waisglass et al., 2006). However, to our knowledge, no studies have specifically explored behavioral associations with inflammatory gastrointestinal and dermatological diseases.

Measuring the association between GI and skin discomfort and domestic cat behavior would raise awareness for owners and clinicians, and allow for better management and treatment of animals with relevant medical and behavioral disorders. The study reported below investigates whether cats with inflammatory gastrointestinal and dermatological disorders display behavior profiles that are different from those of healthy cats. I hypothesize that domestic cats with chronic inflammatory disorders would display more behavioral signs of anxiety than healthy cats.

The second aim of this project is to investigate behavioral effects of corticosteroid treatment in cats. Previous research in dogs found a positive association between glucocorticoid treatment and anxiety (Klinck et al., 2008). Additional research in rats reports that sustained increased levels of

glucocorticoids raises anxiety (Kellendonk et al., 2002). This suggests that increased anxiety could be a potential unintended side effect of prolonged corticosteroid treatment. I explored whether the same effect is present in cats and hypothesized that cats treated with corticosteroids would exhibit more anxious behaviors than both healthy cats and cats with inflammatory disease who were not treated with steroids.

Materials and Methods

This study was reviewed by the Institutional Review Board of the University of Pennsylvania on November 21, 2022 and was exempted from Institutional Review Board oversight. The study was approved by Penn Vet's Privately Owned Animal Protocol (POAP) committee.

Study Population

I identified cats from existing feline patient records at Penn Vet's Ryan Hospital database that had been diagnosed with particular inflammatory medical disorders that are of interest to us. These include gastrointestinal disorders (inflammatory bowel disease, chronic enteropathy, colitis) and dermatological disorders (atopic dermatitis, allergic dermatitis, atopic skin syndrome, chronic pruritus, eosinophilic granuloma complex, pemphigus foliaceus, chronic otitis externa). All cats in the inflammatory group had been treated for their GI or skin disorder within 1 month prior to my contacting them. I also identified cats with no known medical conditions who had been diagnosed as healthy by a veterinarian to make up the control group.

We chose to focus on gastrointestinal and dermatological disorders for several reasons. First, previous research has shown that the gut microbiota influences behavior via an immune-mediated response, and it has been suggested that the skin microbiota may also influence behavior (Collins et al., 2009; Sherwin et al., 2019; Rosenthal et al., 2011; Onaolapo et al., 2020). Additionally, there is some clinical evidence that chronic GI or skin inflammation is associated with behavior

changes in other species (Camps et al., 2019). Finally, GI and skin diseases are present in a substantial percentage of cats treated in behavior clinics and both conditions are relatively easy to identify, because owners and clinicians can observe episodes of vomiting, diarrhea, anorexia, and indiscriminate eating, as well as skin rashes, lesions, inflammation, and excessive scratching.

Study inclusion criteria were that the cat being evaluated was at least 1.5 years of age and had a veterinary diagnosis of inflammatory GI or dermatological disease or a healthy diagnosis. We selected the minimum age requirement, ensuring that all cats in the study were adults, because temperament is more stable in adult cats (Bradshaw, 2012). Additionally, the person completing the survey was required to be 18 years of age or older. We guaranteed participants that the results of the study would not disclose any identifying information about them or their pet during publication and presentations.

Data Collection

Because chronic medical conditions may lead to subtle behavioral changes over time, and cat behavior naturally changes in a clinical setting, we felt that it was necessary to assess the cats' behavior in their home environments. We chose to ask pet owners to complete the Feline Behavioral Assessment & Research Questionnaire (Fe-BARQ©) (Duffy, et al., 2017). The Fe-BARQ is a validated behavioral assessment survey, which has been shown to provide information on the temperament and behavior history of cats. The survey is available online, easily accessible for users, and takes 10-15 minutes to complete.

The Fe-BARQ Questionnaire includes a total of 100 questions that ask cat owners to rate how often their cat performs a specific behavior. The owners rank the frequency of each behavior on a five-point ordinal scale ranging from “never” to “always” (0 to 4) (never = 0, seldom = 1, sometimes = 2, usually = 3, always = 4). These 100 questions measure 38 separate categories of cat activity, behavior, and interactions with humans and other animals at home. I selected 25 of the behavior categories to compare between groups (activity, sociability to people, vocalizations, purring, attention-seeking behavior, aggression to strangers, aggression to owner, fear of novelty, separation problem behaviors, trainability, prey interest, location preferences, compulsive grooming, other compulsive behaviors, inappropriate elimination, elimination preferences, crepuscular activity, agitation, loud vocalizations, spraying, picked up / held, adapts to changes, loud noise response, scratching on inappropriate objects, and kneading behavior).

I contacted (by email) the owners of the cats I had identified to ask if they were willing to participate in the project by completing the Fe-BARQ for their cat. When pet owners responded positively, I sent them the POAP approved owner consent form and Fe-BARQ survey completion instructions. Participants completed the online questionnaire from their homes and entered our study’s unique access code so that their responses came directly to us.

Data Analysis

To compare the Fe-BARQ survey results of cats with inflammatory GI and skin conditions to those of healthy controls, I used the SPSS Statistics software and

performed the Mann Whitney U test. I considered a value of $p < .05$ to be significant.

Results

To collect Fe-BARQ data about both healthy cats and cats with inflammatory disease, I distributed 63 surveys to cat owners, and I received 51 completed surveys (80%) that met inclusion criteria (aged 18 months or older and (1) a diagnosed inflammatory gastrointestinal or dermatological disorder or (2) diagnosed as healthy by a veterinarian). The responses included 21 GI Disease, 18 Dermatology, and 12 healthy. Additionally, we had a repository of data Fe-BARQ recorded from cats diagnosed as healthy. I used data from 46 healthy cats from this resource to make up a robust control group.

Dividing our subjects into groups by inflammatory status

To begin the analysis, it was necessary to divide our subjects by inflammatory status. First, I categorized the cats into two groups. The healthy group (n = 58) included cats that had been examined by a veterinarian within 3 months prior to survey completion and had no known medical conditions. The inflammatory group (n = 39) included cats that had a veterinary diagnosis of inflammatory gastrointestinal or dermatological disease.

Subsequently, I divided inflammatory subjects into two subgroups according to the source of the inflammation: (1) cats with a dermatological disease diagnosis (n = 17) and (2) cats with a gastrointestinal disease diagnosis (n = 22). I compared each of these subgroups to the healthy group (n = 58).

I recorded all medications used to treat the cats in our study, which had been noted in their patient medical records. At the time of survey completion, 18 cats in the inflammatory group (46%) were being treated with medications that had the potential to affect behavior, including corticosteroids (n = 12) as well as anti-anxiety/seizure medications, and antidepressants (n = 9). No cats in the healthy group were being treated with medications.

Because some of the medications used in the inflammatory group are known to have psychoactive effects, I wanted to determine whether treatment with these medications would alter our results. To assess this, I removed the cats from the inflammatory group that were receiving anti-anxiety drugs and antidepressants (Gabapentin and Mirtazapine) and re-sorted the remaining subjects into three new groups: inflammatory cats not treated with mood-altering drugs (n = 30), dermatology cats not treated with mood-altering drugs (n = 14), and GI cats not treated with mood altering drugs (n = 16). I compared each of these groups to the healthy group (n = 58) separately to determine whether the presence of these mood-altering drugs affected our results.

Then, to establish whether treatment with corticosteroids affected our results, I further sorted the inflammatory group into two additional subgroups: cats treated with corticosteroids (n = 12) and cats not treated with corticosteroids (n = 27). I first compared the steroid group to the non-steroid group, and then compared the steroid group to the healthy group and the non-steroid group to the healthy group.

Finally, I removed the cats who were treated with anti-anxiety drugs and antidepressants from the non-steroid group and compared this group (n = 19) to

the healthy group. Only one cat in the steroid group was also receiving a mood-altering drug, and therefore, I did not run the analysis of the steroid group without mood-altering drugs.

Results from the Comparison of Behavioral Measures between Groups

Comparison of behavior in healthy cats and those with Inflammatory disease

The first comparison between the healthy group (n = 58) and the inflammatory group (n = 39) revealed three statistically significant differences. The inflammatory group displayed higher mean ranks in the Fe-BARQ categories of purring (p = .042), trainability (p = .021), and compulsive grooming (p = <.001), while the remaining 22 categories showed no statistically significant difference between groups (Table 1).

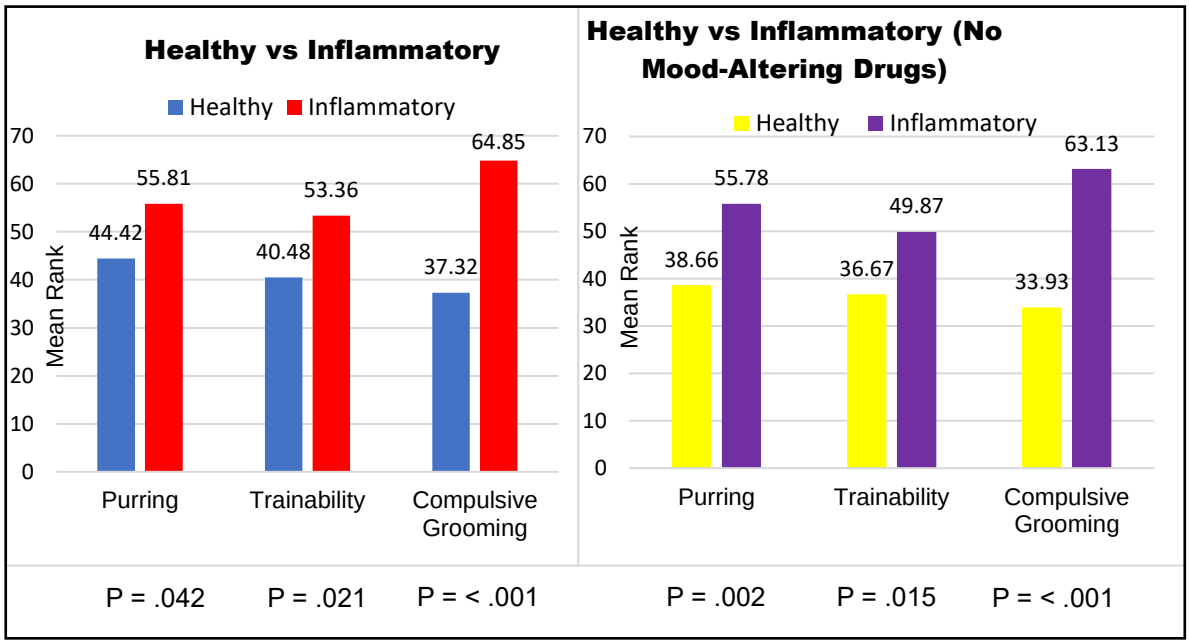
When I removed cats treated with mood-altering drugs from the inflammatory group and performed the comparison again, the same three categories (purring (p = .002), trainability (p = .015), and compulsive grooming (p = <.001)) showed statistically significant differences between groups (Table 1) and the confidence level increased (Figure 1).

Table 1. Comparison of behavioral measures between healthy cats and those with inflammatory disease

	Independent Samples Mann Whitney U Test. p < .05						
	Healthy (n = 58) vs Inflammatory (n = 39)			Healthy (n= 58) vs Inflammatory (No Mood-Altering Drugs) (n = 30)			
Fe-BARQ Category	Healthy Mean Rank	Inflammatory Mean Rank	Significance	Healthy Mean Rank	Inflammatory (no MAD) Mean Rank	Significance	Retain or Reject Null Hypothesis.
Activity	48.95	49.08	0.982	44.59	44.32	0.961	Retain
Sociability to People	34.48	38.21	0.451	29.61	34.63	0.276	Retain
Vocalizations	52.95	43.13	0.091	46.48	40.67	0.309	Retain
Purring	**44.42**	**55.81**	**0.042**	**38.66**	**55.78**	**0.002**	**Reject**
Attention Seeking	48.67	49.49	0.885	44.33	44.83	0.928	Retain
Aggression to Strangers	36.90	36.14	0.847	32.96	31.98	0.788	Retain
Aggression to Owner	45.91	53.60	0.165	43.50	46.43	0.587	Retain
Fear of Novelty	45.80	51.15	0.342	41.19	47.82	0.231	Retain
Separation Behavior	39.54	42.58	0.548	35.93	37.30	0.776	Retain
Trainability	**40.48**	**53.36**	**0.021**	**36.67**	**49.87**	**0.015**	**Reject**
Prey Interest	44.63	46.74	0.703	41.39	41.71	0.953	Retain
Location Preferences	48.32	46.35	0.727	42.89	43.20	0.956	Retain
Compulsive Grooming	**37.32**	**64.85**	**0.000**	**33.93**	**63.13**	**0.000**	**Reject**
Other Compulsive Behaviors	44.83	52.75	0.163	41.25	47.91	0.234	Retain
Inappropriate Elimination	48.61	49.58	0.829	43.91	45.65	0.693	Retain
Elimination Preferences	40.02	39.97	0.991	35.56	36.72	0.784	Retain
Crepuscular Activity	50.51	44.40	0.281	45.38	40.00	0.335	Retain
Agitation	47.00	44.61	0.614	42.69	39.33	0.466	Retain
Loud Vocals	48.45	49.82	0.803	43.87	45.72	0.734	Retain
Sprays	48.41	49.87	0.600	44.09	45.30	0.652	Retain
Picked Up / Held	47.78	50.82	0.571	44.96	43.62	0.797	Retain
Adapts to Changes	49.78	44.28	0.306	44.73	39.83	0.353	Retain
Loud Noise Response	49.23	48.65	0.918	45.59	42.40	0.564	Retain
Scratching	47.68	49.69	0.716	45.01	42.08	0.588	Retain
Kneading	49.18	48.73	0.937	44.50	44.50	1.000	Retain

Comparison of Mann Whitney U Test mean rank results between healthy cats and cats with inflammatory disease across 25 behavioral measures from the Fe-BARQ survey. Significant results are bolded. MAD = mood altering drugs.

Figure 1. Significant behavioral measures between healthy cats and those with inflammatory disease with and without mood-altering drugs



Cats with inflammatory disease showed significantly higher Fe-BARQ score mean ranks than healthy cats in the categories of purring, trainability, and compulsive grooming. These results remained consistent when cats receiving mood-altering drugs were removed from the analysis. Statistics performed by Mann Whitney U test comparing inflammatory (with and without MADs) to healthy for each Fe-BARQ category. MAD = mood-altering drugs.

Comparison of behavior in healthy cats and those with dermatological disease.

In order to assess if there was a difference in behavioral measures between types of inflammatory disease, I separated the inflammatory group into two subgroups: dermatological disease (n = 17) and gastrointestinal disease (n = 22), and I compared each of those subgroups individually to the healthy group (n = 58).

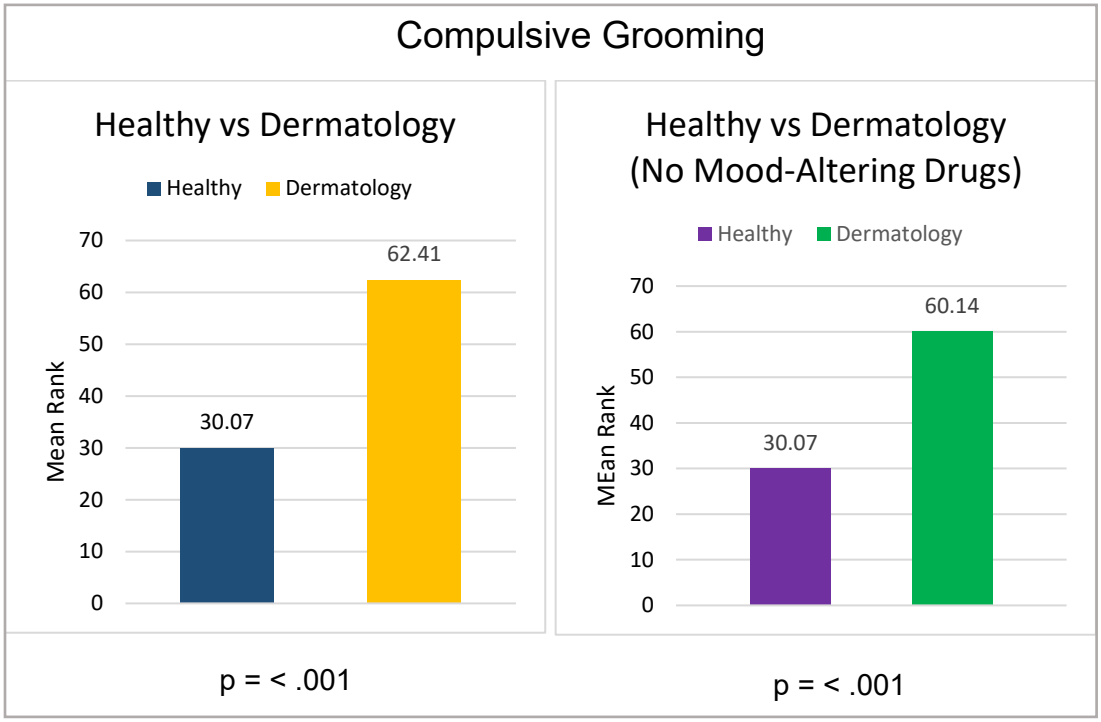
The dermatology group showed a higher mean rank score for compulsive grooming behavior than the healthy group ($p = <.001$). The remaining 24 categories showed no statistically significant differences between groups. This result remained the same when I removed animals who were treated with mood-altering drugs (Table 2). The categories of trainability and purring, both of which had statistically significant differences in the initial inflammatory–healthy group comparison, were no longer significant in the dermatology–healthy comparison.

Table 2. Comparison of behavioral measures between healthy cats and those with dermatological disease

Independent Samples Mann Whitney U Test p < .05							
	Healthy (n = 58) vs Dermatology (n = 17)			**Healthy (n = 58) vs Dermatology (No Mood-Altering Drugs) (n = 14)**			
Fe-BARQ Category	Healthy Mean Rank	Dermatology Mean Rank	Significance	Healthy Mean Rank	Dermatology (no MAD) Mean Rank	Significance	Retain or Reject Null Hypothesis.
Activity	39.41	33.21	0.302	38.25	29.25	0.149	Retain
Sociability to People	26.26	24.03	0.608	24.77	22.18	0.552	Retain
Vocalizations	39.50	32.88	0.269	37.88	30.79	0.253	Retain
Purring	36.09	44.53	0.146	34.49	44.82	0.086	Retain
Attention Seeking	36.60	42.76	0.289	35.47	40.79	0.378	Retain
Aggression to Strangers	26.90	24.21	0.412	25.00	23.29	0.612	Retain
Aggression to Owner	36.84	41.94	0.370	36.41	36.89	0.934	Retain
Fear of Novelty	37.42	35.62	0.753	35.96	33.68	0.701	Retain
Separation Behavior	29.27	31.79	0.597	28.63	28.11	0.914	Retain
Trainability	32.52	42.59	0.070	31.14	42.25	0.052	Retain
Prey Interest	35.45	35.65	0.972	35.05	30.04	0.385	Retain
Location Preferences	37.27	34.00	0.569	35.91	31.43	0.450	Retain
Compulsive Grooming	**30.07**	**62.41**	**0.000**	**30.07**	**60.14**	**0.000**	**Reject**
Other Compulsive Behaviors	35.38	44.62	0.114	34.88	40.57	0.346	Retain
Inappropriate Elimination	38.73	35.50	0.462	36.87	34.96	0.680	Retain
Elimination Preferences	29.16	30.57	0.748	27.69	29.23	0.738	Retain
Crepuscular Activity	38.63	31.65	0.229	37.18	28.79	0.162	Retain
Agitation	36.57	32.18	0.351	35.11	29.79	0.273	Retain
Loud Vocals	37.70	39.03	0.815	37.14	33.86	0.576	Retain
Sprays	37.14	40.94	0.210	36.02	38.50	0.406	Retain
Picked Up / Held	38.68	35.68	0.582	37.76	31.29	0.250	Retain
Adapts to Changes	37.63	32.85	0.384	35.58	32.71	0.611	Retain
Loud Noise Response	37.39	40.09	0.639	35.53	40.54	0.403	Retain
Scratching	38.90	32.79	0.276	38.11	27.43	0.065	Retain
Kneading	37.38	40.12	0.639	36.06	38.32	0.709	Retain

Comparison of Mann Whitney U Test mean rank results between healthy cats and cats with dermatological disease (with and without mood-altering drugs) across 25 behavioral measures from the Fe-BARQ survey. Significant results are bolded. MAD = mood altering drugs.

Figure 2. Significant behavioral measures between healthy cats and those with dermatological disease with and without mood-altering drugs.



Cats with dermatological disease showed significantly higher Fe-BARQ score mean ranks than healthy cats in the category of compulsive grooming. These results remained consistent when cats receiving mood-altering drugs were removed from the analysis. Statistics performed by Mann Whitney U test comparing dermatology (with and without MADs) to healthy for each Fe-BARQ category. MAD = mood-altering drugs.

Comparison of behavior in healthy cats and those with gastrointestinal disease

I observed a similar result in the initial comparison between cats with gastrointestinal disorders and healthy cats The GI group showed a higher incidence of compulsive grooming behavior when compared to the healthy group, and no other categories revealed differences between groups (Table 3).

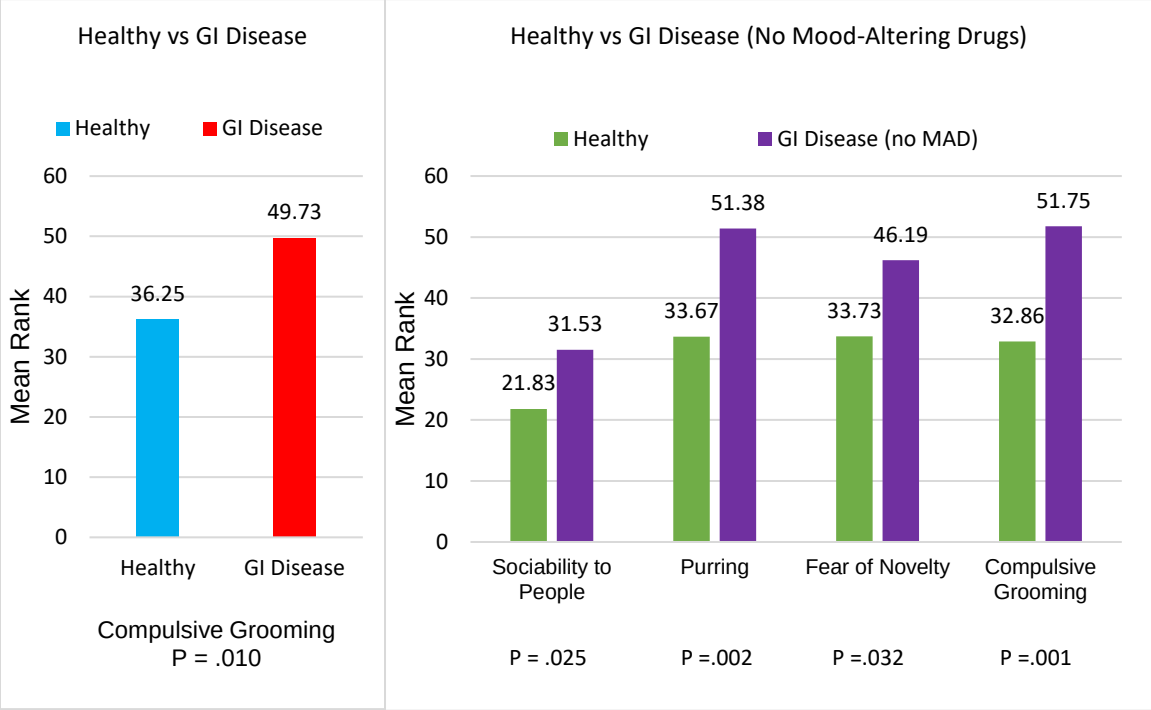
Interestingly, when I removed the cats treated with mood-altering drugs from the GI group, the difference between groups in the compulsive grooming category remained statistically significant (in fact, the significance increased tenfold, from $p = .010$ to $p = .001$), and three additional categories showed statistically significant differences between groups (sociability to people ($p = .025$), purring ($p = .002$), and fear of novelty ($p = .032$). The GI group had a higher mean rank than the healthy group in all four behavior categories (Table 3; Figure 3).

Table 3. Comparison of behavioral measures between healthy cats and those with gastrointestinal disease.

Independent Samples Mann Whitney U Test p = < .05									
Healthy (n = 58) vs Gastrointestinal Disease (n = 22)					**Healthy (n = 58) vs Gastrointestinal Disease (No Mood-Altering Drugs) (n = 16)**				
Fe-BARQ Category	Healthy Mean Rank	GI Mean Rank	Sig.	Retain or Reject Null Hypothesis.	Fe-BARQ Category	Healthy Mean Rank	GI (no MAD) Mean Rank	Sig.	Retain or Reject Null Hypothesis.
Activity	39.04	44.34	0.362	Retain	Activity	35.84	43.5	0.207	Retain
Sociability to People	25.23	32.16	0.115	Retain	**Sociability to People**	**21.83**	**31.53**	**0.025**	**Reject**
Vocalizations	42.95	34.05	0.124	Retain	Vocalizations	38.10	35.31	0.644	Retain
Purring	37.84	47.52	0.084	Retain	**Purring**	**33.67**	**51.38**	**0.002**	**Reject**
Attention Seeking	41.57	37.68	0.492	Retain	Attention Seeking	38.36	34.38	0.500	Retain
Aggression to Strangers	27.50	28.81	0.719	Retain	Aggression to Strangers	25.46	25.59	0.969	Retain
Aggression to Owner	38.56	45.61	0.198	Retain	Aggression to Owner	36.59	40.78	0.459	Retain
Fear of Novelty	36.88	46.16	0.097	Retain	**Fear of Novelty**	**33.73**	**46.19**	**0.032**	**Reject**
Separation Behavior	31.76	33.91	0.650	Retain	Separation Behavior	28.80	31.34	0.594	Retain
Trainability	34.46	44.68	0.060	Retain	Trainability	32.03	42.53	0.062	Retain
Prey Interest	36.18	39.18	0.586	Retain	Prey Interest	33.34	38.6	0.356	Retain
Location Preferences	39.05	38.89	0.977	Retain	Location Preferences	34.98	39.50	0.436	Retain
Compulsive Grooming	**36.25**	**49.73**	**0.010**	**Reject**	**Compulsive Grooming**	**32.86**	**51.75**	**0.001**	**Reject**
Other Compulsive Behaviors	38.46	42.33	0.495	Retain	Other Compulsive Behaviors	35.38	40.77	0.366	Retain
Inappropriate Elimination	39.38	43.45	0.372	Retain	Inappropriate Elimination	36.53	41.00	0.346	Retain
Elimination Preferences	33.36	32.24	0.787	Retain	Elimination Preferences	30.36	30.88	0.905	Retain
Crepuscular Activity	40.38	37.25	0.577	Retain	Crepuscular Activity	36.7	35.81	0.880	Retain
Agitation	37.43	37.67	0.961	Retain	Agitation	34.58	34.23	0.945	Retain
Loud Vocals	40.25	41.16	0.868	Retain	Loud Vocals	36.23	42.09	0.308	Retain
Sprays	40.78	39.77	0.681	Retain	Sprays	37.57	37.25	0.904	Retain
Picked Up / Held	38.59	45.52	0.201	Retain	Picked Up / Held	36.7	40.41	0.508	Retain
Adapts to Changes	40.15	36.11	0.441	Retain	Adapts to Changes	37.15	32.06	0.354	Retain
Loud Noise Response	41.34	38.27	0.583	Retain	Loud Noise Response	39.56	30.03	0.103	Retain
Scratching	37.78	45.75	0.144	Retain	Scratching	35.90	40.91	0.379	Retain
Kneading	41.30	38.39	0.606	Retain	Kneading	37.94	35.91	0.730	Retain

Comparison of Mann Whitney U Test mean rank results between healthy cats and cats with gastrointestinal disease (with and without mood-altering drugs) across 25 behavioral measures from the Fe-BARQ survey. Significant results are bolded. MAD = mood altering drugs.

Figure 3. Significant behavioral measures between healthy cats and those with gastrointestinal disease with and without mood-altering drugs.



Cats with gastrointestinal disease showed significantly higher Fe-BARQ score mean ranks than healthy cats in the category of compulsive grooming. When I removed cats receiving mood-altering drugs from the analysis, three additional categories showed significance (sociability, purring, fear of novelty). Statistics performed by Mann Whitney U test comparing cats with gastrointestinal disease (with and without MADs) to healthy cats for each Fe-BARQ category. MAD = mood-altering drugs.

Comparison of behavior in cats treated with or without corticosteroids

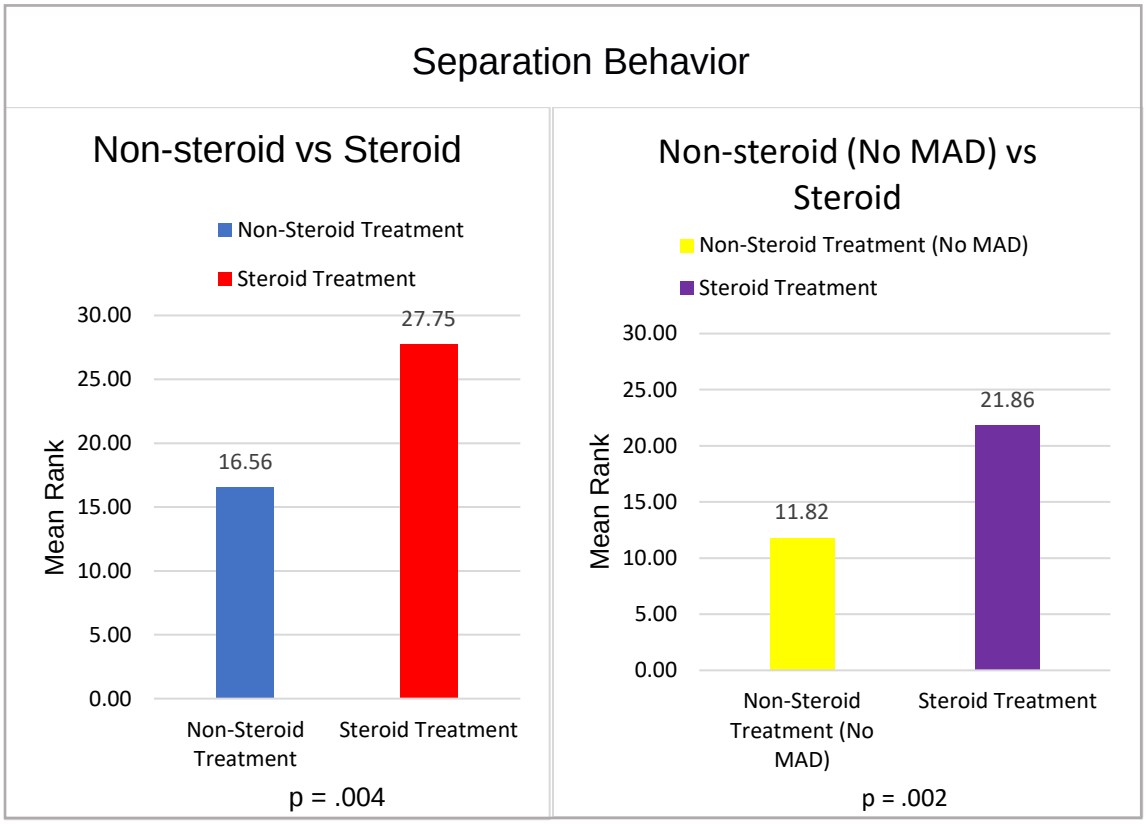
Within the inflammatory group (n = 39), 12 cats (30.7%) received corticosteroid treatment for their GI or dermatology condition. To assess whether treatment with corticosteroids affected cat behavior in the inflammatory group, I compared Fe-BARQ scores from inflammatory cats not treated with corticosteroids (n = 27) to those receiving corticosteroid treatment (n = 12). The inflammatory group contained cats with both GI and dermatology conditions. The steroid treatment group had a significantly higher incidence of separation problem behaviors than the non-steroid treatment group ($p = .004$). Nine cats in the non-steroid group were being treated with anti-anxiety or antidepressant medications. To establish whether steroid treatment was in fact causing the difference in separation behavior between groups or whether mood-altering medications were affecting the results, I removed the cats receiving mood altering drugs. The result remained the same, and the significance increased ($p = .002$) (Table 4; Figure 4).

Table 4. Comparison of behavioral measures between inflammatory disease cats treated with and without corticosteroids

Independent Samples Mann Whitney U Test p < .05							
	Non-Steroid Treatment (n = 27) vs Steroid Treatment (n = 12)			**Non-Steroid Treatment (No Mood-Altering Drugs) (n = 19) vs Steroid Treatment (n = 12)**			
Fe-BARQ Category	Non-Steroid Mean Rank	Steroid Mean Rank	Significance	Non-Steroid (no MAD) Mean Rank	Steroid Mean Rank	Significance	Retain or Reject Null Hypothesis.
Activity	20.19	19.58	.893c	15.97	14.68	.703c	Retain
Sociability to People	18.65	23.04	.271c	14.82	16.68	.582c	Retain
Vocalizations	19.41	21.33	.642c	15.11	16.18	.767c	Retain
Purring	20.3	19.33	.822c	16.42	13.91	.471c	Retain
Attention Seeking	19.67	20.75	.799c	15.03	16.32	.703c	Retain
Aggression to Strangers	17.81	23.17	.174c	13.47	19	.103c	Retain
Aggression to Owner	18.70	22.92	.298c	13.92	18.23	.200c	Retain
Fear of Novelty	20.24	19.46	.845c	16.13	14.41	.611c	Retain
Separation Behavior	**16.56**	**27.75**	**.004c**	**11.82**	**21.86**	**.002c**	**Reject**
Trainability	20	20	1.000c	15.21	16	.832c	Retain
Prey Interest	18.14	20.79	.491c	13.44	19.55	.220c	Retain
Location Preferences	18.85	22.58	.358c	14.45	17.32	.395c	Retain
Compulsive Grooming	19.06	22.13	.443c	14.5	17.23	.420c	Retain
Other Compulsive Behaviors	17.35	24.17	.081c	12.67	18.82	.061c	Retain
Inappropriate Elimination	20.39	19.13	.753c	15.89	14.82	.767c	Retain
Elimination Preferences	18.28	17.3	.815c	14.31	13.39	.781c	Retain
Crepuscular Activity	21.2	17.29	.327c	16.13	14.41	.611c	Retain
Agitation	19.72	18.95	.849c	14.76	15.45	.839c	Retain
Loud Vocals	21.48	16.67	.233c	16.82	13.23	.287c	Retain
Sprays	20.89	18.00	.480c	16.37	14.00	.497c	Retain
Picked Up / Held	20.69	18.46	.578c	15.68	15.18	.899c	Retain
Adapts to Changes	19.81	20.42	.893c	14.96	16.45	.672c	Retain
Loud Noise Response	20.06	19.88	.964c	15	16.36	.703c	Retain
Scratching	18.74	22.83	.313c	13.39	19.14	.085c	Retain
Kneading	17.96	24.58	.098c	13.79	18.45	.171c	Retain

Comparison of Mann Whitney U Test mean rank results between inflammatory cats treated with steroids and inflammatory cats treated without steroids (with and without mood-altering drugs) across 25 behavioral measures from the Fe-BARQ survey. Significant results are bolded. MAD = mood altering drugs.

Figure 4. Significant behavioral measures between inflammatory disease cats treated with steroids and those receiving non-steroid treatment (with and without mood-altering drugs).



Cats treated with corticosteroids showed significantly higher Fe-BARQ score mean ranks than cats not treated with steroids in the category of separation behavior. This result remained significant when I removed cats receiving mood-altering drugs from the analysis. Statistics performed by Mann Whitney U test comparing inflammatory disease cats treated with corticosteroids to inflammatory disease cats treated without steroids (with and without MADs) for each Fe-BARQ category. MAD = mood-altering drugs.

Comparison of behavior in healthy cats and those treated with corticosteroids

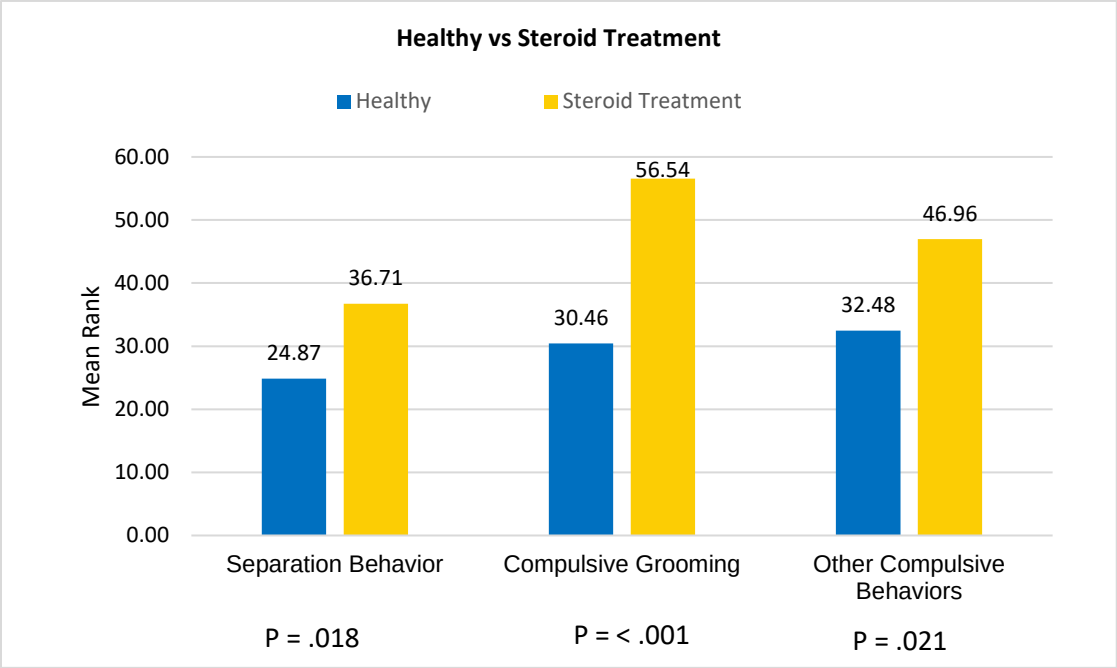
To establish whether steroid treatment affected the differences we observed in the initial comparison between the healthy group and the inflammatory group, I compared the scores from the steroid group (n = 12) to the healthy group (n = 58) and then the non-steroid group (n = 27) to the healthy group. The analysis revealed that the steroid group scored higher in the categories of separation problem behaviors ($p = .018$), compulsive grooming ($p = < .001$), and other compulsive behaviors ($p = .021$) than the healthy group (Table 5; Figure 5).

Table 5. Comparison of behavioral measures between healthy cats and inflammatory disease cats treated with corticosteroids.

Independent Samples Mann Whitney U Test p < .05				
Healthy (n = 58) vs Steroid Treatment (n = 12)				
Fe-BARQ Category	Healthy Group Mean Rank	Steroid Group Mean Rank	Significance	Retain or Reject Null Hypothesis.
Activity	35.77	34.21	0.809	Retain
Sociability to People	21.23	27.88	0.135	Retain
Vocalizations	36.12	32.5	0.573	Retain
Purring	34.48	40.42	0.340	Retain
Attention Seeking	35.16	37.17	0.746	Retain
Aggression to Strangers	22.71	25.75	0.406	Retain
Aggression to Owner	33.58	44.79	0.066	Retain
Fear of Novelty	33.99	36.88	0.639	Retain
Separation Behavior	**24.87**	**36.71**	**0.018**	**Reject**
Trainability	30.88	39.54	0.143	Retain
Prey Interest	32.13	36.83	0.431	Retain
Location Preferences	33.14	37.96	0.431	Retain
Compulsive Grooming	**30.46**	**56.54**	**0.000**	**Reject**
Other Compulsive Behaviors	**32.48**	**46.96**	**0.021**	**Reject**
Inappropriate Elimination	35.63	34.88	0.876	Retain
Elimination Preferences	27.7	26.6	0.811	Retain
Crepuscular Activity	35.9	27.96	0.201	Retain
Agitation	32.90	30.59	0.657	Retain
Loud Vocals	36.39	31.21	0.391	Retain
Sprays	35.91	33.50	0.353	Retain
Picked Up / Held	35.66	34.71	0.872	Retain
Adapts to Changes	34.63	31.13	0.548	Retain
Loud Noise Response	35.65	34.79	0.890	Retain
Scratching	33.34	42.88	0.109	Retain
Kneading	33.96	42.96	0.151	Retain

Comparison of Mann Whitney U Test mean rank results between healthy cats and inflammatory cats treated with steroids across 25 behavioral measures from the Fe-BARQ survey. Significant results are bolded.

Figure 5. Significant behavioral measures between healthy cats and inflammatory disease cats treated with corticosteroids.



Cats treated with steroids showed significantly higher Fe-BARQ score mean ranks than healthy cats in the categories of separation behaviors, compulsive grooming, and other compulsive behaviors. Statistics performed by Mann Whitney U test comparing inflammatory disease cats treated with steroids to healthy cats for each Fe-BARQ category.

Comparison of behavior in healthy cats and those treated without corticosteroids

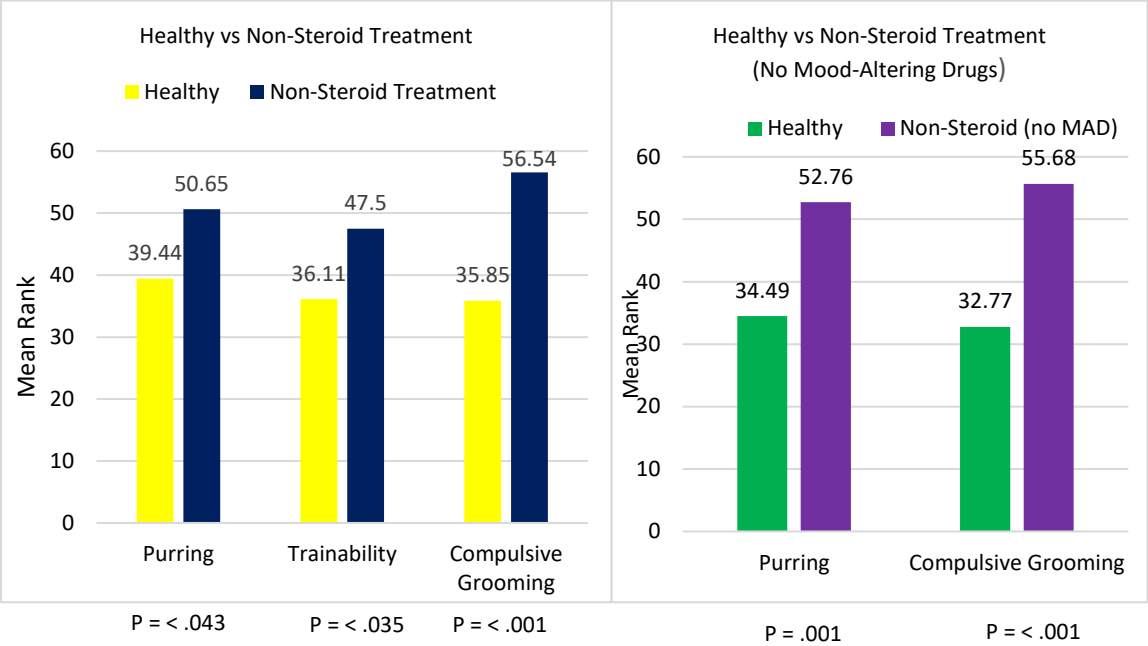
I then looked at cats with inflammatory disease who were not treated with steroids and compared their behavioral measures to healthy cats. The inflammatory group contained cats with both GI and dermatology disease. The comparison between the non-steroid and healthy groups showed that the non-steroid group had a higher frequency of purring ($p = .043$), trainability ($p = .035$), and compulsive grooming ($p = < .001$) than the healthy group. When I removed the cats treated with mood-altering drugs, the non-steroid group scored higher than the healthy group in the categories of purring ($p = .001$) and compulsive grooming ($p = < .001$), however trainability was no longer significantly different between groups ($p = .053$) (Table 6; Figure 6).

Table 6. Comparison of behavioral measures between healthy cats and inflammatory disease cats not treated with corticosteroids.

Independent Samples Mann Whitney U Test p < .05									
Healthy (n = 58) vs Non-Steroid Treatment (n = 27)					**Healthy (n = 58) vs Non-Steroid Treatment (No Mood-Altering Drugs) (n = 17)**				
Fe-BARQ Category	Healthy Mean Rank	Non-Steroid Mean Rank	Sig.	Retain / Reject Null Hypothesis	Fe-BARQ Category	Healthy Mean Rank	Non-Steroid Mean Rank	Sig.	Retain / Reject Null Hypothesis.
Activity	42.68	43.69	0.861	Retain	Activity	38.71	39.89	0.841	Retain
Sociability to People	30.26	30.8	0.905	Retain	Sociability to People	25.56	28.13	0.555	Retain
Vocalizations	46.33	35.85	0.067	Retain	Vocalizations	40.68	33.87	0.247	Retain
Purring	**39.44**	**50.65**	**0.043**	**Reject**	**Purring**	**34.49**	**52.76**	**0.001**	**Reject**
Attention Seeking	43.02	42.96	0.992	Retain	Attention Seeking	39.19	38.42	0.894	Retain
Aggression to Strangers	31.69	28.94	0.427	Retain	Aggression to Strangers	28.38	24.53	0.234	Retain
Aggression to Owner	41.83	45.52	0.496	Retain	Aggression to Owner	39.42	37.71	0.755	Retain
Fear of Novelty	40.31	45.5	0.349	Retain	Fear of Novelty	36.15	43.45	0.199	Retain
Separation Behavior	36.17	33.19	0.529	Retain	Separation Behavior	32.96	26.66	0.176	Retain
Trainability	**36.11**	**47.5**	**0.035**	**Reject**	Trainability	33.15	43.79	0.053	Retain
Prey Interest	39.5	39.5	1.000	Retain.	Prey Interest	36.99	33.08	0.482	Retain
Location Preferences	43.18	38.07	0.357	Retain	Location Preferences	38.18	35.53	0.640	Retain
Compulsive Grooming	**35.85**	**56.54**	**0.000**	**Reject**	**Compulsive Grooming**	**32.77**	**55.68**	**0.000**	**Reject**
Other Compulsive Behaviors	41.35	43.42	0.711	Retain	Other Compulsive Behaviors	38.07	37.78	0.960	Retain
Inappropriate Elimination	42.48	44.11	0.712	Retain	Inappropriate Elimination	38.4	40.84	0.591	Retain
Elimination Preferences	34.82	35.32	0.905	Retain	Elimination Preferences	31.02	32.67	0.699	Retain
Crepuscular Activity	43.11	39.70	0.541	Retain	Crepuscular Activity	38.79	35.68	0.587	Retain
Agitation	41.10	39.31	0.703	Retain	Agitation	37.47	33.79	0.435	Retain
Loud Vocals	41.56	46.09	0.407	Retain	Loud Vocals	37.76	42.79	0.370	Retain
Sprays	42	45.15	0.279	Retain	Sprays	38.21	41.42	0.276	Retain
Picked Up / Held	41.61	45.98	0.410	Retain	Picked Up / Held	38.97	39.08	0.984	Retain
Adapts to Changes	43.15	38.13	0.338	Retain	Adapts to Changes	38.94	33.34	0.297	Retain
Loud Noise Response	43.09	42.81	0.961	Retain	Loud Noise Response	39.96	36.08	0.497	Retain
Scratching	42.75	41.96	0.884	Retain	Scratching	40.42	32.74	0.167	Retain
Kneading	44.69	39.37	0.340	Retain	Kneading	40.20	35.34	0.397	Retain

Comparison of Mann Whitney U Test mean rank results between healthy cats and inflammatory cats not treated with corticosteroids (with and without mood-altering drugs) across 25 behavioral measures from the Fe-BARQ survey. Significant results are bolded. MAD = mood-altering drugs.

Figure 6. Significant behavioral measures between healthy cats and inflammatory disease cats not treated with corticosteroids (with and without mood-altering drugs).



Inflammatory disease cats treated without corticosteroids showed significantly higher Fe-BARQ score mean ranks than healthy cats in the categories of purring, trainability, and compulsive grooming. When I removed cats receiving mood-altering drugs from the analysis, the difference between groups in the categories of purring and compulsive grooming remained significant, and trainability was no longer significant. Statistics performed by Mann Whitney U test comparing inflammatory disease cats receiving non-steroid treatment (with and without MADs) to healthy cats for each Fe-BARQ category. MAD = mood-altering drugs.

Discussion

Below, I describe my interpretation for each difference observed between groups. The first comparison between the healthy and inflammatory groups showed that cats with inflammatory disease scored higher than healthy cats in purring ($p = .042$), trainability ($p = .021$), and compulsive grooming ($p = <.001$)

Purring – Domestic cats use a purr sound to communicate with other cats and also with humans, and they have even been observed purring when they are alone (Bradshaw et al., 2012). Although we often interpret purring as a sign of contentment, previous research has revealed that cats purr to solicit comfort and attention from others (McComb et al., 2009). Purring is an innate vocalization that cats use to communicate from birth. Queens initially use a purr to communicate with their newborn kittens until their ear canals open. Kittens also purr to request food, warmth, and protection from their mother, and the queen responds to these vocal signals by meeting their needs (Ley, 2015). Cats continue to use purring as a means of communicating their needs to their human caregivers. In these situations, cats may purr not due to contentment, but to express their desire to be cared for (McComb et al., 2009).

Additionally, the act of purring may produce a comforting or healing effect to the cat itself (von Muggenthaler, 2001). Cats have been observed to purr when they are distressed, sick, and/or in pain; indeed, sick and injured cats have even been observed to purr as they are dying (Bradshaw et al., 2012). In these circumstances, some researchers believe that the function of purring is to self-

soothe and promote healing during times of physical and emotional distress (von Muggenthaler, 2001). Domestic cats purr at frequencies between 25 and 150 Hz, with the strongest frequencies being at 25 Hz, 50 Hz, and 100 Hz. These frequencies correspond to the exact vibrational frequencies shown to promote bone growth, muscle growth, and wound healing, and also to reduce pain and edema (Chen et al., 1994). This suggests that, by purring, distressed, sick, or injured cats may be attempting to self-comfort or heal.

The Fe-BARQ asks pet owners to measure the likelihood of their cat to purr in two circumstances (1) the cat purrs when stroked or petted, and (2) the cat purrs when sitting/lying on someone's lap (Duffy et al., 2017).

In this study, cats with inflammatory conditions purred significantly more than healthy cats. I interpret this result to indicate a state of increased discomfort and/or stress in the inflammatory group. I suggest that the higher incidence of purring in the inflammatory group relates to the cats' attempt to self-soothe or to solicit comfort from their owners.

Additional results from this study support this interpretation. Treatment with psychoactive medications reduced the incidence of purring in the inflammatory group. When I removed the cats receiving antidepressants and anti-anxiety drugs from the analysis, the difference of purring mean rank between the healthy and inflammatory group grew, as did the statistical significance of the result. If purring in the context of this study were an indication of contentment, then I would expect to see a higher incidence of purring in cats receiving antidepressants and anti-

anxiety medications. However, I observed the opposite: the highest scores for purring occurred in inflammatory group cats not receiving antidepressants and anti-anxiety medications.

When I divided the inflammatory group into two subgroups related to the type of inflammatory disorder (dermatology or GI disease), purring mean ranks were no longer significantly different between the dermatology group and the healthy group (with and without psychoactive drugs). However, when I compared the GI disease group to the healthy group, purring mean rank was initially not significant, but when I removed the cats receiving psychoactive medications from the GI group, I found that GI cats without anti-anxiety / antidepressant treatment purred significantly more than healthy cats ($p = .002$). This further emphasizes that treatment with anti-anxiety and antidepressant drugs reduced the rate of purring in cats with inflammatory conditions. Because psychoactive medications reduce purring in cats with inflammatory disease, I conclude that purring positively correlates with stress in cats.

Corticosteroid treatment also had a notable effect on purring behavior. Interestingly, when I separated the inflammatory group into steroid and non-steroid treatment groups, I found that cats treated with corticosteroids showed no significant difference in purring compared to healthy cats, however, cats not treated with steroids had a significantly higher incidence of purring than healthy cats. This reduced rate of purring associated with steroid treatment suggests that treatment with steroids reduces the physical discomfort associated with

inflammatory disease and therefore also reduces the cats' need to self-soothe due to physical discomfort.

Additionally, the difference in mean rank between the non-steroid and healthy groups increased even more when I removed cats treated with antidepressants and anti-anxiety drugs. Cats with inflammatory disease that were not treated with corticosteroids or psychoactive medications had the highest rate of purring when compared to healthy cats. This suggests that cats experiencing discomfort due to inflammatory conditions make a greater attempt to self-soothe or solicit comfort than healthy cats.

The study is limited to a certain extent by a lack of context for some of the behaviors measured. For example, the questionnaire does not give us any context about the cat's body language while purring. Body language is a key communication tool for cats, and some cats continue to purr even when their body language conveys that they are becoming stressed, frustrated, or angry with their situation or their interactions with others (Bradshaw, 2012). Additionally, the survey does not provide information relating to the nature of the purr sound itself (e.g., relaxed or urgent). McComb et al. (2009) showed that the sound of the purr changes when the cat is soliciting attention – these purr sounds contain a high-pitched element, which humans identify as sounding urgent or anxious. Knowing the cats' body language while purring (relaxed or alert) and the sound quality of the vocalizations themselves (relaxed or urgent), would improve the accuracy of the assessment.

Trainability - This study has revealed a positive correlation between inflammatory GI and skin disease and higher trainability. The category of Trainability in the Fe-BARQ measures how well the cat (1) comes when called, (2) readily responds to simple verbal commands (out, in, quiet, down, up, no, lie down, etc.), and (3) attends and listens closely to everything [the owners] say or do (Duffy et al., 2017). Cats in the inflammatory group scored significantly higher in the category of trainability than healthy cats.

The Fe-BARQ does not ask owners to report the methods used to train their cats. Positive reinforcement training methods involve the owner giving the cat a reward when it responds appropriately to a verbal cue. Food treats work well as a reinforcer for training cats who are highly food motivated, while some cats are enticed by attention and affection from their owner, such as play or petting/stroking (Bradshaw & Ellis, 2016). Additionally, corticosteroids can increase appetite, in fact they were historically used as appetite stimulants in cats, but have been generally phased out for this purpose due to other drug effects (Agnew et al., 2014).

It is possible that the measure of trainability in this study relates to the cat's motivation for food and/or affection. This would suggest that cats with inflammatory disease are more likely to be highly food-motivated than healthy cats and/or they are more likely to desire attention and affection from their owners than healthy cats. Owners providing food and affection to the cats can be means of providing comfort, and the inflammatory group's increased desire for comfort may result in increased trainability. This is consistent with the higher rate of purring in the inflammatory group, which, as discussed earlier, suggests cats with inflammatory

disorders are seeking more comfort from their owners. It is also possible that cats selected for personality traits that make them easier to train (more interactive, more food-motivated, etc.) are more likely to have inflammatory GI and skin disease.

The differences I observed in trainability between groups remained consistent regardless of the presence of antidepressants / anti-anxiety drugs. This indicates that psychoactive or mood-altering drugs (MAD) do not affect trainability, which suggests that the difference between groups is related to physical inflammation, but not specifically to anxiety or a negative affective state.

While the inflammatory group as a whole (n = 39) scored higher in trainability than healthy cats (n = 58), the difference in trainability between groups no longer crossed the significance threshold ($p < .05$) when I compared the dermatology group (n = 17) to the healthy group ($p = .070$ with MAD and $p = .052$ without MAD) and then the GI disease group (n = 22) to the healthy group ($p = .060$ with MAD and $p = .062$ without MAD).

Steroid treatment, however, did affect trainability. When I divided the inflammatory group into steroid (n = 12) and non-steroid (n = 27) treatment groups, the non-steroid group scored significantly higher than the healthy group in trainability. There was no significant difference between the steroid group and the healthy group. This suggests that inflammation is indeed positively correlated with trainability, because corticosteroid treatments, which reduce inflammation, also reduced cat trainability scores.

Compulsive Grooming – I observed the most consistent difference between groups in the category of compulsive grooming. Cats with inflammatory disorders had a higher rate of compulsive grooming than healthy cats, and this finding remained consistent across all group analyses (Inflammatory–Healthy, Dermatology–Healthy, GI Disease–Healthy, Steroid–Healthy, Non-Steroid–Healthy). I observed the largest differences in mean rank in this category between the dermatology group and the healthy group, with the dermatology group being approximately twice as likely to engage in compulsive grooming behaviors as healthy cats (Figure 2).

The Compulsive Grooming category in the Fe-BARQ measures how often a cat exhibits (1) excessive and intensive grooming (e.g., grooming several times a day for long periods), (2) self-mutilation, hair barbering (pulls fur with teeth, vigorously nibbles and/or licks its body parts), and/or (3) sudden frantic licking or chewing (Duffy et al., 2017).

In cats, excessive or compulsive grooming may stem from an underlying medical disorder or may be a displacement behavior resulting from stress or anxiety (Waisglass et al., 2006, Amat et al., 2016). Compulsive behaviors are abnormal and repetitive behaviors that may have an apparent goal (e.g., grooming) but which interfere with normal function or lead to self-injury. They may initially adequately serve a purpose (such as grooming to alleviate pain or itching), but become compulsive when they are no longer associated with the original context (Landsberg et al., 2013).

It can be difficult to distinguish displacement and compulsive behaviors from those with underlying medical causes. Waisglass et al. (2006) found that 76% of cats referred for treatment of presumed psychogenic alopecia actually had an underlying medical cause. In our study, all cats in the inflammatory group have known medical conditions that are likely to cause physical discomfort. Therefore, the higher incidence of compulsive grooming in the inflammatory group could be a reaction to pain and/or itching associated with skin disease and GI disease.

However, if physical disease were the sole cause of compulsive grooming, then treatment with corticosteroids should mitigate the discomfort associated with inflammation, and therefore, I would expect cats treated with steroids to exhibit lower scores for compulsive grooming than inflammatory cats not treated with steroids. Yet, when I divided the inflammatory group into two subgroups (1) cats treated with corticosteroids and (2) those not treated with steroids, there was no significant difference in the incidence of compulsive grooming between groups. The steroid group and the non-steroid group both had higher scores for compulsive grooming when compared to the healthy group. This suggests that the increased compulsive grooming behavior observed in the inflammatory group is not simply an attempt to reduce physical discomfort.

Overgrooming and self-trauma are documented displacement and compulsive behaviors in cats experiencing chronic stress (Waisglass et al., 2006; Landsberg et al., 2013). Therefore, the increased compulsive grooming scores in the inflammatory group may indicate that these cats are experiencing a higher level of stress than the healthy group.

If the behavior were purely stress-related, then I would expect treatment with psychoactive drugs to reduce the incidence of compulsive grooming. The presence or absence of antidepressants and anti-anxiety drugs did not significantly affect the results between groups — across the board inflammatory disease cats compulsively groomed more than healthy cats, regardless of whether they were receiving psychoactive medications, and the significance for all comparisons was $p = <.001$, except for the initial GI disease vs healthy comparison ($p = .01$). However, in the comparison between the GI disease group and the healthy group, the difference in mean rank of grooming behavior increased between groups and the significance increased tenfold (from $p = .01$ to $p = .001$) when I removed cats receiving psychoactive drugs (Figure 3). This suggests that mood-altering drugs do have a small effect on reducing compulsive grooming behavior for cats with inflammatory GI disease, and therefore that this behavior is at least partly stress-related.

Overall, the results for this category show that cats with inflammatory GI and skin disease engage in compulsive grooming behavior significantly more than healthy cats; however, the scope of this study does not allow us to determine with confidence whether inflammatory cats excessively groom to alleviate physical discomfort or to satisfy an emotional need.

Psychoactive drugs – Several cats in the inflammatory group were being treated with medications that have known psychoactive effects (Gabapentin and Mirtazapine). Mirtazapine (a tetracyclic antidepressant), is commonly prescribed as an appetite stimulant and antiemetic in cats, and it also has a calming or

sedating effect, while Gabapentin (an anticonvulsant) has multiple effects and is commonly used to treat seizures, anxiety, pain, and pruritus in cats (Landsberg et al., 2013). Because these drugs may affect the mood and behavior of cats in our study, I analyzed the data twice for each comparison between groups – first with all cats, including those on mood-altering medications, and then I removed the cats receiving mood-altering medications and ran the analysis again.

I saw the most notable effect of psychoactive drugs in the comparison between the GI disease group and the healthy group. The initial comparison (with psychoactive drugs present) revealed one significant difference between the healthy and GI disease group: the GI group scored higher in compulsive grooming than the healthy group ($p = .010$). However, when I removed cats receiving antidepressants and anti-anxiety drugs and ran the comparison again, three additional categories showed significant differences between groups. This time, in addition to the GI group scoring higher than the healthy group for compulsive grooming ($p = .001$), cats with GI disease had significantly higher scores for sociability to people ($p = .025$), purring ($p = .002$), and fear of novelty ($p = .032$).

As previously discussed, compulsive grooming may be related to physical discomfort, psychological distress, or a combination of both. Cats with GI disease may be excessively grooming to alleviate pain, or they may be overgrooming as a means of coping with stress.

As described above, purring cats attempt to self-comfort or solicit care from owners. This interpretation is further strengthened by the fact that the presence of

psychoactive medication reduced purring behavior to insignificant levels. Cats not treated with psychoactive drugs, however, purred significantly more than healthy cats. Because psychoactive drugs reduced purring, the results suggest that increased purring is indeed associated with stress or anxiety in cats with GI disease.

The GI disease group without mood-altering drugs scored higher in the category of sociability to people than the healthy group. Domestic cats are social animals and often choose to reside in social groups with other cats and/or other species (Bradshaw, 2013). Sociability relates to an individual's tendency to express affiliative behaviors in these social contexts (Finka, 2022). In the Fe-BARQ, the sociability to people category measures how likely the cat is to be comfortable and relaxed among people in social gatherings, being petted by unfamiliar (non-household) person(s), when playing with familiar or unfamiliar children or adults, and how likely the cat is to greet unfamiliar adults or children visiting their home in a friendly manner (sniffs, rubs, purrs, lies on the floor) (Duffy et al., 2017).

GI disease has been associated with extreme, insatiable hunger in cats and can result in increased begging for food and therefore more frequent social interactions with people (Landsberg et al., 2013). This physiological explanation for these results would suggest that sociability to people relates to the cats' attempt to alleviate GI discomfort by soliciting food. However, cats treated with psychoactive medications did not interact with people any more than healthy cats.

Increased social interactions are typically associated with cats experiencing neutral or positive emotional states (Atkinson, 2018; Bradshaw, 2018; Malamed & Sueda, 2020). In contrast, cats experiencing stress or fear are typically less likely to interact, more likely to hide, and more reluctant to play (Ellis, 2018).

Given this understanding of cat social interactions, I would expect cats treated with anti-anxiety drugs and antidepressants (i.e., cats experiencing a positive emotional state) to be more social to people than cats not treated with psychoactive medications. However, the results showed the opposite: I found no significant difference between healthy cats and the GI disease group (which included cats treated with psychoactive medications), but cats not on mood-altering drugs scored higher for sociability to people than healthy cats.

This result raises a number of questions about the function of the feline sociability to people behavior. One interpretation of these results is that interacting with people relieves stress/anxiety in cats, and therefore cats medicated with psychoactive drugs no longer need the comfort provided by social interactions with humans. Because the presence of psychoactive drugs in the GI disease group reduced sociability to people to insignificant levels, this could suggest that mitigating anxious and depressive symptoms through psychoactive therapies (improving mood) decreases sociability to people in cats with GI disease. Alternatively, as both Gabapentin and Mirtazapine can have a sedative effect on cats, it is possible that cats receiving these medications engage in fewer social interactions with people because they are feeling sleepy.

Fear of novelty has been associated with anxiety in many species, including cats. The cognitive bias paradigm works on the premise that judgements are influenced by affective state, and therefore individuals experiencing a negative state of mind are more likely to interpret a neutral stimulus as negative than individuals experiencing a positive state of mind (Mendl et al., 2009). Following this model, we can interpret that when cats react fearfully to novel objects placed in their environment (neutral stimulus), they are experiencing a negative affective state.

The Fe-BARQ classifies fear of novelty as the cat displaying restlessness (active investigation) when its resting area is modified (e.g., objects moved from usual place, changing fabrics/sheets, etc.), as well as restlessness and hypervigilance when unfamiliar objects are introduced into the home.

The presence of psychoactive drugs in the GI disease group reduced fear of novelty behavior to a level that was not significantly different from the healthy group, but cats not treated with mood-altering drugs scored significantly higher for fear of novelty behaviors than healthy cats. Because antidepressant and anti-anxiety treatments mitigate fear of novelty in cats with GI disease, this indicates that cats with GI disease are experiencing negative affective states (greater stress or anxiety) compared to healthy cats. This finding is consistent with previous work in dogs, which found that dogs with inflammatory bowel disease had increased fear of novel stimuli (Monte et al., 2010).

All of these findings highlight that psychoactive medications affect the behavior of cats with inflammatory GI disease, and further support the hypothesis that anxiety is present at a higher rate in the inflammatory group.

Corticosteroids - Although corticosteroids are effective at treating inflammation, steroid treatments can lead to additional problems relating to unexpected side effects. Previous research found that pruritic dogs treated with glucocorticoids displayed more anxiety than dogs who received non-steroid treatments (Klinck et al., 2008). In another preliminary study exploring the behavior of dogs treated with corticosteroids, owners reported that dogs treated with steroids exhibited increased restlessness/nervousness, aggression, and startle response (Notari & Mills, 2010). To explore whether steroids had a similar effect in cats, I looked at how the behavior of inflammatory disease cats treated with corticosteroids differed from those not treated with steroids.

The steroid group showed higher scores for separation problem behaviors than non-steroid group ($p = .004$). This remained consistent when I removed cats treated with psychoactive drugs ($p = .002$), which suggests that difference is related to steroid treatment itself and is not affected by antidepressants and anti-anxiety drugs.

The Fe-BARQ classifies separation problem behaviors as certain behaviors the cat performs when the owner is getting ready to leave the home and after the cat is left alone. Specifically, the survey measures how likely the cat is to become restless, agitated and/or pace, sulk, hide, or slink away when the owner prepares

to leave the home, and if the cat lies down or stays still in the vicinity of the entrance door when the owner prepares to leave the home. It also records if the cat displays restlessness (active investigation), remains still and alert or hypervigilant (constant ear movements and watchful eyes), and vocalizes by crying or meowing when it is left alone at home (Duffy et al., 2017).

Separation problems are recognized indicators of fear and anxiety in cats, although separation distress disorders are much better documented in dogs (Schwartz, 2002; Horowitz & Mills, 2010). Because our study showed that cats treated with steroids were more likely to exhibit separation problem behaviors than healthy cats, this suggests that steroid treatment in cats correlates with increased anxiety.

When I compared cats treated with steroids to healthy cats, separation problem behaviors remained significant, with the steroid group showing higher rates of this behavior than the healthy group ($p = .018$). This result further strengthens the interpretation that steroid treatment is associated with increased anxiety. Additionally, the steroid group showed higher scores for compulsive grooming ($p = < .001$), and also higher rates of other compulsive behaviors ($p = .021$) than the healthy group.

Compulsive grooming, as previously discussed, can be caused by a medical condition or indicate anxiety and stress in cats (Tynes & Sinn, 2014). Because steroid treatment led to increased scores for this behavior, it is unlikely to be related to physical discomfort caused by inflammation (which corticosteroids would

mitigate). A previous study suggests that excessive grooming behavior may also be related to separation distress in cats (Schwartz, 2002). Because both separation behaviors and compulsive grooming behaviors are significantly higher in cats treated with steroids, this further supports the interpretation that corticosteroid treatment increases anxiety.

The results also revealed that cats treated with steroids are more likely to perform other compulsive behaviors than healthy cats. This Fe-BARQ category is distinct from compulsive grooming and includes locomotor behaviors, such as abnormal repetitive movements (e.g., pacing or walking in circuits), and also hallucinatory behaviors, such as freezing and staring intently at “nothing”, or staring intently at people (Duffy et al., 2017). Many medical conditions can cause or contribute to repetitive locomotor and hallucinatory behaviors, so it is important to consider a physical reason for these results. Pacing and circling have been associated with medical conditions that cause pain (Overall & Dunham, 2002). Similarly, hallucinatory behaviors have been associated with seizures and other neurological disorders (Landsberg et al., 2013). Abnormal repetitive behaviors that are not caused by medical conditions are likely a result of anxiety due to feelings of conflict or frustration (Tynes & Sinn, 2014). In this study, only cats in the inflammatory group that were treated with steroids exhibited significant levels of other compulsive behaviors. Because this behavior was absent from inflammatory cats not treated with steroids, this suggests that corticosteroid treatment is associated with compulsive locomotor and/or hallucinatory behaviors.

Separation problem behavior, compulsive grooming, and other compulsive behaviors are all indicative of increased anxiety. Separation problem behavior and other compulsive behaviors are only present at significant levels in cats treated with corticosteroids. This suggests that there is a positive correlation between corticosteroid treatment and increased anxiety in cats.

When compared to the healthy group, the non-steroid group (which included both GI and dermatology disease subjects) displayed the same behavior profile as the inflammatory group as a whole, scoring higher in the categories of purring ($p = .043$), trainability ($p = .035$), and compulsive grooming ($p = < .001$). However, in the initial comparison (Inflammatory vs healthy), mood-altering drugs did not appear to affect the results; the inflammatory group scored higher in all three behaviors regardless of the presence of antidepressants and anti-anxiety drugs. In the non-steroid vs healthy comparison, mood-altering drugs do show an effect. When I removed cats treated with psychoactive medications and ran the comparison again, purring ($p = .001$) and compulsive grooming ($p = < .001$) both remained significant, and trainability no longer showed significance ($p = .053$). This suggests that psychoactive drugs do affect trainability, possibly by improving the cats' mood and desire to interact with humans.

A limitation of this study is the relatively small sample size for the inflammatory group ($n = 39$) and healthy group ($n = 58$), and therefore I acknowledge that the results of my comparisons between groups for each category may not be representative of all inflammatory and healthy populations.

Additionally, given that this is a survey-based study, the results are based on owners reporting their perception of their cats' activities and behaviors. This subjective self-reporting leads to potential unconscious inaccuracies. Owners may also misinterpret their cats' abnormal or negative behavior as normal or positive. For example, a lack of understanding of cat body language may cause owners to interpret an aggressive interaction as a playful one, and owners might view tail chasing and pouncing on "imaginary" things as cute, playful behaviors, when they could actually be abnormal repetitive behaviors. Nonetheless, owners who continuously interact with and observe their cats in their home environments are uniquely positioned to provide valuable information about cat behavior that cannot be collected in a clinical environment.

Further limitations include comorbidities and medications. Many of the cats in the inflammatory group had comorbidities that were distinct from inflammatory GI disease or skin disease but which may have an effect on the results of this study. There were also many cats in the inflammatory group being treated with medications other than the corticosteroids and psychoactive medications considered relevant to this study.

Future work should examine our results further with larger sample sizes for all groups, attempt to correct for comorbidities and other medication effects, and attempt to use more objective measures to interpret the motivation for these behaviors.

Conclusion

This study revealed that cats with inflammatory GI and skin diseases display behavior profiles that are different from those of healthy cats. The results showed a positive correlation between inflammatory GI and skin disease and anxious / comfort-soliciting behavior in cats. Additionally, there was a higher incidence of separation problem behaviors and compulsive behaviors in corticosteroid-treated cats, suggesting that corticosteroid treatment increases anxiety in cats. The findings of this study do not rule out the possibility of a medical cause for these behaviors, however, we cannot assume that these behavioral differences result solely from an attempt to alleviate physical discomfort. It is beyond the scope of the study to conclusively determine whether these behaviors are a reaction to physical discomfort, emotional distress, or a combination of the two. Additional studies are needed to explore the effect of GI and dermatological disease and corticosteroid treatments on cat behavior.

References

1. Agnew, W., & Korman, R. (2014). Pharmacological appetite stimulation: rational choices in the inappetent cat. *Journal of feline medicine and surgery*, 16(9), 749-756.
2. Amat M. Camps T. & Manteca X. (2016). Stress in owned cats: behavioural changes and welfare implications. *Journal of Feline Medicine and Surgery* 577–86. https://doi.org/10.1177/1098612X15590867
3. Atkinson, Trudi author. *Practical Feline Behaviour : Understanding Cat Behaviour and Improving Welfare /*. Oxfordshire, UK ; Boston, MA :: CABI,, 2018. Print.
4. Bercik, P., Denou, E., Collins, J., Jackson, W., Lu, J., Jury, J., Deng, Y., Blennerhassett, P., Macri, J., McCoy, K. D., Verdu, E. F., & Collins, S. M. (2011). The intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice. *Gastroenterology*, 141(2), 599–609.e6093. https://doi.org/10.1053/j.gastro.2011.04.052
5. Berteselli GV, Servidaq F, DallAra P, et al. (2005). Evaluation of the immunological, stress and behavioral parameters in dogs (Canis familiaris) with anxiety-related disorders. In: Mills D, Levine E, (Eds.). *Current issues and research in veterinary behavioral medicine*. (pp. 18–22). Purdue University Press.
6. Bhatia, V., & Tandon, R. K. (2005). Stress and the gastrointestinal tract. *Journal of gastroenterology and hepatology*, 20(3), 332–339. https://doi.org/10.1111/j.1440-1746.2004.03508.x
7. Bradshaw J. (2013). *Cat Sense: How the new feline science can make you a better friend to your cat*. Basic Books.
8. Bradshaw J. (2018). Normal feline behaviour: … and why problem behaviours develop. *Journal of feline medicine and surgery*, *20*(5), 411–421. https://doi.org/10.1177/1098612X18771203
9. Bradshaw, J. W. S., Casey, R. A., Brown, S. L. (2012). *The Behaviour of the Domestic Cat*. 2nd Edition. CAB International, Wallingford U.K.
10. Bradshaw, J. and Ellis, S. (2016) *The Trainable Cat: How to Make Life Happier for You and Your Cat*. Basic Books, New York.
11. Camps, T., Amat, M., & Manteca, X. (2019). A review of medical conditions and behavioral problems in dogs and cats. *Animals*, *9*(12), 1133.

12. Chen, L. P., Han, Z. B., & Yang, X. Z. (1994). *Zhonghua wai ke za zhi [Chinese Journal of Surgery]*, 32(4), 217–219.

13. Collins, S. M., Denou, E., Verdu, E. F., & Bercik, P. (2009). The putative role of the intestinal microbiota in the irritable bowel syndrome. *Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver*, 41(12), 850–853. https://doi.org/10.1016/j.dld.2009.07.023

14. Dreschel NA. (2009) Anxiety, fear, disease and lifespan in domestic dogs. *Journal of Veterinary Behaviour*. 4:249–50.

15. Duffy, D. L., de Moura, R. T. D., & Serpell, J. A. (2017). Development and evaluation of the Fe-BARQ: A new survey instrument for measuring behavior in domestic cats (Felis s. catus). *Behavioural Processes*, 141, 329-341.

16. Ellis SL. Recognising and assessing feline emotions during the consultation: History, body language and behaviour. *Journal of Feline Medicine and Surgery*. 2018 May;20(5):445-456. doi: 10.1177/1098612X18771206. PMID: 29706094.

17. Frank. (2014). Recognizing Behavioral Signs of Pain and Disease. *The Veterinary Clinics of North America.*, *44*(3), 507–524. https://doi.org/10.1016/j.cvsm.2014.01.002

18. Finka, L. R. (2022). Conspecific and Human Sociality in the Domestic Cat: Consideration of Proximate Mechanisms, Human Selection and Implications for Cat Welfare. *Animals*, *12*(3), 298. MDPI AG. http://doi.org/10.3390/ani12030298.

19. Horwitz, D. (1997). Behavioral and environmental factors associated with elimination behavior problems in cats: a retrospective study. *Applied Animal Behaviour Science,* 52:1–2. 129-137. ISSN 0168-1591. https://doi.org/10.1016/S0168-1591(96)01073-8.

20. Horwitz D. & Mills D. (2010). BSAVA manual of canine and feline behavioural medicine (2nd ed.). British Small Animal Veterinary Association.

21. Kellendonk, C., Gass, P., Kretz, O., Schütz, G., & Tronche, F. (2002). Corticosteroid receptors in the brain: gene targeting studies. *Brain research bulletin*, 57(1), 73–83. https://doi.org/10.1016/s0361-9230(01)00638-4

22. Klinck M. P. Shofer F. S. & Reisner I. R. (2008). Association of pruritus with anxiety or aggression in dogs. *Journal of the American Veterinary Medical Association* 1105–11. https://doi.org/10.2460/javma.233.7.1105

23. Klinck, M. P., Frank, D., Guillot, M., & Troncy, E. (2012). Owner-perceived signs and veterinary diagnosis in 50 cases of feline osteoarthritis. *The Canadian veterinary journal = La revue veterinaire canadienne*, 53(11), 1181–1186

24. Landsberg, G. M., Hunthausen, W. L., Ackerman, L. J., & Landsberg, G. M. (2013). *Behavior problems of the dog and ca*t. Third edition. Edinburgh: Saunders/Elsevier.

25. Ley, J.M. (2015). Feline communication. In Rodan, I. & Heath, S. (Eds.). Feline behavioral health and welfare. (pp. 24-33). Elsevier.

26. Malamed R. & Sueda K.L.C. (2020). The Language of Meow: Feline Phonics from Nose to Tail. In M.E. Herron, D.F. Horwitz, & C. Siracusa (Eds.), *Decoding Your Cat* (pp. 1-26). Houghton Mifflin Harcourt.

27. McComb, K., Taylor, A. M., Wilson, C., & Charlton, B. D. (2009). The cry embedded within the purr. *Current biology* : CB, 19(13), R507–R508. https://doi.org/10.1016/j.cub.2009.05.033

28. Mendl M. Burman O. H. P. Parker R. M. A. & Paul E. S. (2009). Cognitive bias as an indicator of animal emotion and welfare: emerging evidence and underlying mechanisms. *Applied Animal Behaviour Science* 161–181. https://doi.org/10.1016/j.applanim.2009.02.023

29. Merola, I., & Mills, D. S. (2016). Behavioural signs of pain in cats: an expert consensus. *PLoS One*, *11*(2), e0150040

30. Mills, D. S., Demontigny-Bédard, I., Gruen, M., Klinck, M. P., McPeake, K. J., Barcelos, A. M., Hewison, L., Van Haevermaet, H., Denenberg, S., Hauser, H., Koch, C., Ballantyne, K., Wilson, C., Mathkari, C. V., Pounder, J., Garcia, E., Darder, P., Fatjó, J., & Levine, E. (2020). Pain and Problem Behavior in Cats and Dogs. *Animals: an open access journal from MDPI*, *10*(2), 318. https://doi.org/10.3390/ani10020318

31. Monte F, Basse C, Lynch A. (2010). Stress as a factor in inflammatory bowel disease; pilot study to investigate whether affected dogs differ from unaffected controls in their response to novel stimuli. In: Hamburg, Germany: Proceedings of the 2010 European Veterinary Behavior Meeting. (pp. 46–9).

32. Notari L, Mills D. (2010). The effects of exogenous corticosteroids on dog behaviour; a preliminary study. *Journal of Veterinary Behavior*. 5(1):63-63 DOI:10.1016/j.jveb.2009.10.006

33. Onaolapo, O. J., Onaolapo, A. Y., & Olowe, A. O. (2020). The neurobehavioral implications of the brain and microbiota interaction. *Frontiers in Bioscience-Landmark*, 25(2), 363-397.

34. Overall, K. L., & Dunham, A. E. (2002). Clinical features and outcome in dogs and cats with obsessive-compulsive disorder: 126 cases (1989-2000). *Journal of the American Veterinary Medical Association*, 221(10), 1445–1452. https://doi.org/10.2460/javma.2002.221.1445

35. Rosenthal, M., Goldberg, D., Aiello, A., Larson, E., & Foxman, B. (2011). Skin microbiota: microbial community structure and its potential association with health and disease. *Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases*, 11(5), 839–848. https://doi.org/10.1016/j.meegid.2011.03.022

36. Schwartz S (2002). Separation anxiety syndrome in cats: 136 cases (1991–2000). *Journal of the American Veterinary Medical Association*. 220, 1028–1033

37. Sherwin, E., Bordenstein, S. R., Quinn, J. L., Dinan, T. G., & Cryan, J. F. (2019). Microbiota and the social brain. *Science*. 366(6465), eaar2016. https://doi.org/10.1126/science.aar2016

38. Stella JL, Lord LK, Buffington T. (2011). Sickness behaviours in response to unusual environmental events in healthy cats and cats with FIC. *Journal of the American Veterinary Medical Association*.1:67–73.

39. Stella JL, Buffington CAT (2014). Individual and environmental effects on health and welfare. In: Turner DC, Bateson p (eds). *The domestic cat – the biology of its behaviour*. 3rd ed. Cambridge University Press. (pp. 185-200).

40. Tynes, & Sinn, L. (2014). Abnormal Repetitive Behaviors in Dogs and Cats. *The Veterinary Clinics of North America*. 44(3), 543–564. https://doi.org/10.1016/j.cvsm.2014.01.011