ANALYSIS OF A QUANTITATIVE BEHAVIORAL ASSESSMENT PROGRAM TO IDENTIFY AND TREAT ABNORMAL BEHAVIORS IN CAPTIVE PRIMATES

A Dissertation
Presented to
The Academic Faculty

By

Allison L. Martin

In Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy in Psychology

Georgia Institute of Technology

May 2016

ANALYSIS OF A QUANTITATIVE BEHAVIORAL ASSESSMENT PROGRAM TO IDENTIFY AND TREAT ABNORMAL BEHAVIORS IN CAPTIVE PRIMATES

Approved by:

Dr. Terry L. Maple, Advisor
School of Psychology
Georgia Institute of Technology

Dr. James S. Roberts
School of Psychology
Georgia Institute of Technology

Dr. M. Jackson Marr
School of Psychology
Georgia Institute of Technology

Dr. Corrine K. Lutz
Southwest National Primate Research Center
Texas Biomedical Research Institute

Dr. Mollie A. Bloomsmith
Yerkes National Primate Research Center
Emory University

Date Approved: March 17, 2016

I imagine that everyone who completes a dissertation needs some support along the way. To help me reach my goal, my parents made countless sacrifices, and my friends generously gave their time. This dissertation is dedicated to everyone who brought me a meal, wore out my dogs, wrangled goats, kept me laughing, and otherwise helped to make this degree possible.

-Sully

ACKNOWLEDGEMENTS

This work was supported in part by the NIH/OD grant P51-OD-011132 to the Yerkes National Primate Research Center (YNPRC). I thank my advisor, Dr. Terry Maple, and my mentors, Dr. Jack Marr and Dr. Mollie Bloomsmith for their guidance and encouragement throughout my graduate career. I am grateful to my committee members, Dr. James Roberts and Dr. Corrine Lutz, for their support and direction through this dissertation project. I recognize the personnel in the Behavior Management Unit for their tireless work to improve the welfare of the primates at YNPRC and thank them for supporting and encouraging me throughout my time there. I also thank Jessica Clevenger for her assistance with data summary and Susan Martin for her assistance with manuscript preparation.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

SUMMARY

Facilities housing non-human primates are required to make provisions for their psychological wellbeing, which may include monitoring animals for signs of decreased wellbeing such as the presence of abnormal behaviors or alopecia. By analyzing archival behavioral data collected by the Behavior Management Unit at the Yerkes National Primate Research Center (YNPRC), I aimed to identify behavioral predictors of self-wounding and alopecia and to evaluate the effectiveness of current treatments in reducing abnormal behavior and alopecia in rhesus macaques (*Macaca mulatta*). The behaviors of self-biting and hair plucking (conditional logistic regression, $p < .05$) as well as floating limb and self-oral behaviors (Mantel-Haenszel chi-square tests, $p < .05$) were identified as behavioral predictors of self-wounding. Fear behaviors were associated with an increased risk of developing alopecia (Mantel-Haenszel chi square, $p < .05$). An inverse relationship was found between alopecia and stereotypic locomotor behaviors such as pacing, with animals who displayed these behaviors being less likely to develop significant hair loss (conditional logistic regression, $p < .05$). Overall, the type of treatment provided (e.g., additional foraging opportunities, the provision of toys, or the provision of visual barriers) did not predict improvement in levels of abnormal behavior or alopecia (logistic regression, $p > .05$). The results of these analyses add to the literature on self-wounding and alopecia and will allow refinement of the quantitative behavioral monitoring system at YNPRC such that more at-risk animals can be identified and treated prior to the development of abnormal or harmful behaviors.

CHAPTER 1: INTRODUCTION

Researchers in the field of captive primate management have accumulated a large body of applied research that examines the causes of and treatments for abnormal behaviors displayed by captive non-human primates (NHP). Robert Yerkes' and Harry Harlow's early contributions helped to define the field (e.g., Harlow & Harlow, 1962; Yerkes, 1925), and the science surrounding the study of captive primate behavior continues to grow. As of 2003, 59% of primate research facilities in the United States employed a behavioral scientist tasked with overseeing the behavior management and wellbeing of laboratory-housed primates (Baker, Weed, Crockett, & Bloomsmith, 2007). Public concerns about the welfare of captive primates, increasing research illustrating the detrimental effects of stress on the usefulness of primates as a research model (Garner, 2005), and other factors have led to increasing regulations regarding the housing and care of captive primates.

The United States Department of Agriculture (1991) requires facilities housing NHP to provide environmental enrichment and to make other provisions to enhance the psychological wellbeing of captive primates. While the best measures of psychological wellbeing are still debated, an absence of harmful abnormal behaviors is generally considered to be one component of wellbeing (National Research Council, 1998). The *Guide for the Care and Use of Laboratory Animals* emphasizes the importance of monitoring animals to identify the emergence of any abnormal behaviors as well as the importance of reviewing and assessing environmental enrichment programs to assure that they are meeting their goal to increase animal wellbeing (National Research Council of the National Academies, 2011). In alignment with these goals, the Behavior Management Unit (BMU) at the Yerkes National Primate Research Center (YNPRC) developed a quantitative system to monitor rates of abnormal behavior in the colony and to identify and treat animals with behaviors of concern. The aim of this study was to evaluate and improve the effectiveness and efficiency of this program.

Abnormal Behaviors in Captive Primates

Abnormal behaviors, often broadly defined as behaviors that differ qualitatively or quantitatively from those expressed by primates in natural settings, include topographies such as bizarre posturing, floating limb, self-biting, self-clasping, eye-poking, stereotyped pacing, bouncing in place, rocking, and coprophagy (Erwin & Deni, 1979). There is a large body of scientific literature examining factors that lead to the development of abnormal behaviors in NHP. Beginning in the 1950's, Harry Harlow's lab demonstrated the impact of various rearing conditions on the development of abnormal behaviors in NHP (e.g., Harlow & Harlow, 1962; Meyer, Novak, Bowman, & Harlow, 1975; Mitchell, Raymond, Ruppenthal, & Harlow, 1966; also see Novak, Kelly, Bayne, & Meyer, 2012 and Novak, Meyer, Lutz, & Tiefenbacher, 2006 for reviews). As reviewed by Novak et al. (2012), the factors that are known to lead to the development of stereotyped and self-injurious behaviors in NHP include socially-impoverished early rearing conditions (e.g., mother-infant separation, partial or total social isolation, peer-rearing), being housed in individual or socially-impoverished housing as adolescents or adults, exposure to stressors, and genetic factors.

The type and prevalence of abnormal behavior in captive primates varies across species, housing conditions, and other factors. For example, one study found that 89% of the 362 rhesus monkeys (*Macaca mulatta*) individually housed in a research facility displayed at least one abnormal behavior, and that each monkey had an average of 2.3 different abnormal behaviors, with stereotypic pacing as the most common topography of abnormal behavior (Lutz, Well, & Novak, 2003). Similarly, Crast, Bloomsmith, Perlman, Meeker, and Remillard (2014) found that 83% of sooty mangabeys (*Cercocebus atys*) singly housed in a laboratory environment exhibited some form of abnormal behavior, with stereotypic locomotor behaviors also being the most common behavior class in that population. While singly-housed animals have been shown to be more at risk of developing abnormal behaviors (Bayne, Dexter, & Suomi, 1992; Lutz et al., 2003; Rommeck, Anderson, Heagerty, Cameron, & McCowan, 2009; Schapiro, Bloomsmith, Suarez, & Porter, 1996), socially-housed animals are not immune. In a survey of socially-housed prosimians in zoos, 13.2% exhibited some form of stereotypic behavior (Tarou, Bloomsmith, & Maple, 2005). Additionally, abnormal behaviors have been documented in socially-housed, zoo-living chimpanzees (*Pan troglodytes*) (Birkett & Newton-Fisher, 2011). Although there is debate about whether or not some topographies of behavior included in the Birket & Newton-Fisher survey (e.g., coprophagy) should be considered abnormal (see Hopper, Freeman, & Ross, 2016; Ross & Bloomsmith, 2011), 58% of the 40 chimpanzees included in the survey exhibited hair plucking, 53% exhibited rocking, and 20% exhibited self-biting (Birkett & Newton-Fisher, 2011).

These high percentages of captive primates displaying abnormal behaviors certainly warrant concern. However, the relationship between the display of abnormal behavior and the animal's welfare or wellbeing is not always clear. For example, while the development of stereotypies is linked with impoverished environments associated with poor welfare, individual animals living within these sub-optimal environments who display stereotyped behaviors show increased measures of welfare (e.g., decreased corticosteroid levels) as compared with animals within that environment who do not engage in stereotyped behaviors (Mason, 1991a; Mason & Latham, 2004).

In determining the impact of abnormal behaviors on the animal's health and welfare, both the topography of the behavior and its frequency should be taken into account. For example, behaviors such as pacing may only be harmful if performed at levels high enough to interfere with other, more adaptive behaviors. In contrast, a single occurrence of other forms of abnormal behavior (e.g., self-biting) may cause tissue damage and pose an immediate risk to the animal's health (Novak et al., 2012).

Stereotypies, generally defined as repetitive and invariant behavior patterns lacking an obvious goal or function (Mason, 1991b), are the most commonly seen abnormal behaviors in captive primates (e.g., Lutz et al., 2003). Stereotypies are sometimes sub-classified as either whole-body stereotypies such as pacing, flipping, or rocking, or as self-directed stereotypies such as digit-sucking or self-grasping (Lutz et al., 2003). While generally not immediately harmful for the animal, stereotypies are thought to be an indicator of decreased welfare and/or sub-optimal housing conditions (Mason, 1991b; Mason & Latham, 2004) and can become harmful to an animal if displayed at levels that interfere with the expression of species-typical behaviors (Novak et al., 2012).

The most worrisome category of abnormal behavior in captive primates is self-injurious behavior (SIB). This behavioral category includes behaviors that have the potential to cause physical damage to the animal, including self-biting, self-slapping, and head-banging. The most common form of SIB in rhesus monkeys is self-biting of the extremities, which can lead to tissue damage and increased risk of infection (Novak, 2003). Risk factors associated with the development of SIB include being male (Gottlieb, Capitanio, & McCowan, 2013; Lutz et al., 2003), nursery rearing (Gottlieb et al., 2013; Lutz et al., 2003; Rommeck et al., 2009), single housing (Gottlieb et al., 2013; Lutz et al., 2003; Rommeck et al., 2009), indoor housing (Gottlieb et al., 2013), cage position within the room (Gottlieb et al., 2013), and exposure to stressful events such as relocations (Davenport, Lutz, Tiefenbacher, Novak, & Meyer, 2008; Gottlieb et al., 2013; Rommeck et al., 2009) or veterinary procedures (Lutz et al., 2003; Novak, 2003).

Monkeys that exhibit SIB show physiological differences from monkeys who do not exhibit SIB, including lower cortisol levels than control animals, suggesting a dysregulation of the hypothalamic-pituitary-adrenocortical (HPA) axis (Tiefenbacher, Novak, Jorgensen, & Meyer, 2000; Tiefenbacher et al., 2004). There is also evidence that the act of self-biting may be negatively reinforced by the reduction of tension. Rhesus monkeys showed a pattern of increased heart rate just prior to the act of self-biting followed by a quick drop in heart rate immediately following the self-biting (Marinus, Chase, Rasmussen, Jorgensen, & Novak, 1999; Novak, 2003).

Alopecia

While technically not an abnormal behavior, alopecia (or hair loss) is seen in captive primates and often raises welfare concerns, including concerns expressed by regulatory agencies (Luchins et al., 2011). Alopecia in captive NHP can result from many different causes, including aging, seasonal variation, behavioral causes (e.g., hair plucking), hormonal variations, nutritional imbalances, genetic factors, and skin conditions such as inflammation, bacterial infections, or parasitic infections (see Novak

& Meyer, 2009 for review). However, despite having a variety of potential causes, when alopecia is observed in captive NHP, the assumption is often that the hair loss is a result of hair plucking (Luchins et al., 2011).

While alopecia has been found to be correlated with the behavior of hair pulling/plucking (Kroeker, Bellanca, Lee, Thom, & Worlein, 2014; Luchins et al., 2011; Lutz, Coleman, Worlein, & Novak, 2013; Martin, Perlman, & Bloomsmith, 2011), hair plucking was not observed in the majority of animals who presented with hair loss. For example, in a survey of over 1200 primates housed across four national primate research centers, some degree of alopecia was reported in an average of 49% of singly-housed rhesus macaques whereas hair plucking was only observed in less than 8% of animals (Lutz et al., 2013). Similarly, Luchins et al. (2011) found that only 54% of alopecic animals were observed hair plucking.

This may indicate that hair plucking is not the cause of alopecia in many animals. However, behavioral sampling techniques may fail to identify many animals who engage in hair plucking. Studies examining the relationship between hair plucking and alopecia included brief observations conducted during normal husbandry procedures (Kroeker et al., 2014; Lutz et al., 2013; Martin, Perlman, et al., 2011) and/or infrequent (1 - 4 times yearly), brief (5 - 10 minute) focal-animal observations (Lutz et al., 2013) that may miss instances of hair plucking. In the Martin, Perlman, et al. (2011) study, even among animals with alopecia, hair plucking was observed in less than 1% of behavioral observations conducted. Even the relatively long (6 hours per subject) sampling periods analyzed in the Luchins et al. (2011) study may have missed animals who hair-pluck infrequently or, for example, only at night. Thus, it can be very difficult to rule out hair plucking as the cause of any individual animal's hair loss.

Additionally, the relationship between alopecia and psychological wellbeing also remains unclear. While alopecia is anecdotally thought to be correlated with poor psychological wellbeing and stress (Luchins et al., 2011), findings regarding the relationship between stress and hair loss have been mixed. Steinmetz et al. (2006) found that rhesus monkeys with alopecia actually showed lower fecal cortisol levels as compared with controls. However, fecal cortisol levels only reflect adrenocortical activity over a relatively short time period (1 day or less) whereas hair cortisol levels reflect HPA activity over a period of several months and thus may be a more appropriate measure of cortisol levels resulting from chronic stressors (Novak et al., 2014). Novak et al. (2014) studied rhesus macaques across three laboratory facilities and found that macaques with significant (≥ 30%) hair loss did, indeed, have higher hair cortisol concentrations than those with no hair loss. However, this relationship only held for two out of the three facilities, and the direction of the association could not be determined. That is, it could be that environmental stressors increase cortisol and lead to alopecia or it could be that alopecia causes localized changes to the surrounding skin that result in increased hair cortisol levels (Novak et al., 2014). Also of note, the Novak et al. study only included rhesus macaques (*n* = 99) with no behavioral evidence of hair plucking, while Steinmetz et al.'s sample (*n* = 60) did not control for behavioral causes.

It is clear more research is needed to fully understand the relationship between alopecia, stress, and welfare. If alopecia is an indicator of poor psychological wellbeing, one might expect to see a correlation between alopecia and the display of abnormal behaviors. However, in a previous exploratory analysis, we found no significant relationship between alopecia and abnormal behaviors other than hair plucking (Martin, Perlman, et al., 2011). Thus, more research is needed into the etiology of alopecia in captive primates and its relationship to psychological wellbeing.

Treatment Effectiveness

At present, a hypothetical behavior manager presented with a monkey exhibiting a particular topography of abnormal behavior has a variety of treatment options from which to choose. These treatments include providing animals with social opportunities; increasing human contact in the form of feeding, playing or grooming; positive reinforcement training to increase cooperation with and reduce the stress associated with husbandry and veterinary procedures; increasing cage size; providing environmental enrichment such as the use of puzzle feeders or forage boards; and pharmacological interventions. However, all of these potential treatments have shown, at best, mixed results in reducing abnormal behaviors (for reviews, see Coleman, Bloomsmith, Crockett, Weed, & Schapiro, 2012; Lutz & Novak, 2005; and Novak et al., 2012).

For example, while some studies have shown that providing animals with environmental enrichment such as toys, forage boards, or puzzle feeders results in the reduction of abnormal behaviors (Bayne et al., 1991; Bloomsmith, Alford, & Maple, 1988; Kessel & Brent, 1998), other studies have found no effect (Byrne & Suomi, 1991; Fekete, Norcross, & Newman, 2000; Line, Morgan, & Markowitz, 1991; Schapiro & Bloomsmith, 1995; Spring, Clifford, & Tomkol, 1997), and one study even found an increase in stereotypic behavior at certain time points after the provision of feeding enrichment devices (Gottlieb et al., 2011). The factors affecting the effectiveness of environmental enrichment to reduce abnormal behavior remain unclear. Further confusing the matter is the fact that any changes seen in behavior may only be short-term. For example, Novak, Kinsey, Jorgensen, and Hazen (1998) found that abnormal behaviors were significantly reduced in rhesus macaques in the time period immediately after puzzle feeders were filled with food. However, 1 hour later, the animals' behaviors returned to baseline levels. Similar results were obtained with the puzzle feeder in the Gottlieb et al. (2011) study.

Similar inconsistencies and complexities are found in the literature examining the effect of other treatments on abnormal behavior, including positive reinforcement training and human interaction (Baker, 2004; Baker, Bloomsmith, Neu, Griffis, & Maloney, 2010; Baker et al., 2009; Coleman & Maier, 2010), cage size (Clarke, Juno, & Maple, 1982; Crockett et al., 1995; Fontenot, Wilkes, & Lynch, 2006; Kaufman, Pouliot, Tiefenbacher, & Novak, 2004), pharmacological interventions (Coble et al., 2010; Fontenot et al., 2005; Kempf et al., 2012; Major et al., 2009; Tiefenbacher et al., 2005), and changes in social housing (Baker et al., 2012; Eaton, Kelley, Axthelm, Iliff-Sizemore, & Shiigi, 1994; Kessel & Brent, 2001; Schapiro, Bloomsmith, Porter, & Suarez, 1996). Overwhelmingly, the research indicates that once an abnormal behavior pattern develops in a captive primate, it is often resistant to current treatment options (Novak et al., 2012).

In addition, the mixed results found in this literature gives a behavior manager very limited information about whether any particular treatment may be more or less effective than another treatment option in treating a specific topography of abnormal behavior. Not all topographies of abnormal behavior respond equally to a given behavioral intervention. For example, in the Novak et al. (1998) study, the provision of a puzzle feeder did result in a short-term reduction in whole-body stereotypic behaviors in rhesus macaques, but self-biting behavior remained unchanged.

In the specific case of the treatment of SIB, very few consistently effective treatments have been identified. While providing environmental enrichment such as toys and foraging devices has been shown to reduce stereotypic behaviors in some cases (e.g., Bayne et al., 1991; Rommeck et al., 2009), the provision of these items has not resulted in significant reduction of self-injurious behaviors in captive NHP (Fekete et al., 2000; Novak et al., 1998; Rommeck et al., 2009). Increasing the size of the monkey's cage also had no effect on rates of SIB (Kaufman et al., 2004). Further, when rhesus macaques (N = 10) with a history of abnormal behaviors were given access to a play cage (which increases both the available space and the level of environmental enrichment), seven out of eight subjects who displayed self-biting in their home cages continued to self-bite in the highly-enriched, play cage environment (Griffis, Martin, Perlman, & Bloomsmith, 2013). To examine the effects of positive reinforcement training on abnormal behavior, Baker et al. (2009) conducted positive reinforcement training sessions to train singly-housed rhesus macaques to perform basic behaviors such as stationing or presenting body parts on cue. This training exposure resulted in no reduction of SIB in these subjects.

The most promising treatments for SIB in NHP involve socialization and medication. Moving macaques from single housing to social housing has been shown to decrease self-biting in some individuals (Line, Morgan, Markowitz, Roberts, & Riddell, 1990; Reinhardt, 1999; Weed et al., 2003). The administration of medications including anxiolytics such as diazepam (Tiefenbacher et al., 2005), guanfacine, a α2A-adrenergic receptor agonist thought to strengthen function in the prefrontal cortex (Macy, Beattie, Morgenstern, & Arnsten, 2009), and serotonergic compounds such as L-tryptophan, fluoxetine and buspirone (Fontenot et al., 2005; Fontenot, Musso, McFatter, & Anderson, 2009; Weld et al., 1998) have all shown some promise in treating SIB in NHP. Although, in some cases, not all animals responded to the medication (e.g., Tiefenbacher et al., 2005), and in others, the improvement was not sustained (Fontenot et al., 2005), was not able to be replicated (Coble et al., 2010), or relapse occurred when the drug was stopped (Macy et al., 2009; Weld et al., 1998). Recently, treatment with extended-release naltrexone, an opioid antagonist, also showed promising results in reducing self-biting (Kempf et al., 2012).

There is also limited and mixed research on the effectiveness of treatment interventions on alopecia in captive primates. Ground substrate has been shown to have an effect on alopecia, with animals housed on grass exhibiting less alopecia than those housed on gravel (Beisner & Isbell, 2008). Foraging enrichment in the form of sunflower seeds in woodchip bedding was found to at least temporarily decrease social hair pulling in group-housed pigtail macaques (*Macaca nemestrina*) (Boccia & Hijazi, 1998), and increased provision of produce in the form of leafy greens was shown to reduce alopecia in socially-housed rhesus macaques (Hannibal, Cassidy, Day, Tatum, & McCowan, 2013). In addition, moving monkeys from single to social housing was shown to decrease alopecia in female long-tailed macaques (*Macaca fascicularis*, Harding, 2013). However, the provision of environmental enrichment in the form of paint rollers and grooming boards did not reduce over-grooming or result in improved hair coats (Runeson, Lee, Crockett, & Bellanca, 2011; Tully, Jenne, & Coleman, 2002).

Triage and Behavioral Correlates

One logistical challenge faced by many behavior managers is the large number of animals under their care (see Baker et al., 2007) and the large percentage of animals displaying abnormal behaviors in some form or another (e.g., Lutz et al., 2003). Behavior managers need a way to triage animals so that they can make behavioral interventions to prevent the most severe behaviors, such as self-wounding, from developing. In addition to demographic and environmental factors such as sex and housing that affect an animal's likelihood of developing abnormal behavior, several studies have identified topographies of behaviors that tend to occur together. Here, most of the attention has been on which behaviors are comorbid with self-injurious behaviors.

Lutz et al. (2003) used a retrospective analysis to find that animals with a veterinary record of wounding engaged in higher levels of self-directed stereotypies (salute, digit-suck, hair pull, and self-grasp) than animals without a wounding history. However, no relationship was found between whole-body stereotypies (pace, bounce, rock, flip, or swing) and self-wounding. In contrast, Rommeck et al. (2009) and Gottlieb et al. (2013) did find a correlation between motor stereotypic behaviors and self-biting in rhesus macaques. Rommeck et al. (2009) found no correlation between self-stimulatory behaviors (self-clasp, self-suck, eye poke/cover, and hair pluck) or alopecia and self-injurious behaviors.

Adding to the literature, Bentson et al. (2010) identified a positive correlation between floating limb behavior and self-biting in laboratory-housed macaques and baboons (*Papio cynocephalus*). While the results of the individual studies varied, combined, these studies suggest that animals displaying certain topographies of abnormal behavior may be more at risk of developing self-injurious behaviors. This suggests that a behavior manager should pay particular attention to animals exhibiting a behavior such as floating limb since these animals seem to be at risk for future wounding.

Study Overview

The aim of the current study was to improve the identification and treatment of captive primates displaying abnormal behaviors. In 2006, the Yerkes National Primate Research Center established a quantitative data collection system to monitor rates of abnormal behavior in our colony and identify and treat animals of concern. This study used these archived data to determine what, if any, behaviors correlate with and predict the development of self-wounding and alopecia in rhesus macaques housed at YNPRC.

Compared with previous studies, my analysis was distinct in its use of a matched experimental design that allowed for the control of factors such as age, sex, and housing status; thus allowing a more narrow focus on the behavioral precursors of wounding and alopecia. Because my data set consisted primarily of one-zero data (such as the presence/absence of behaviors), I chose methodologies ideal for binary data analysis, including conditional logistic regression analysis and principal component analysis based on a tetrachoric correlation matrix. Additionally, by using data collected during the time period leading up to the development of wounding or alopecia, my analysis focused on behaviors that preceded (as opposed to being comorbid with) the development of these conditions. Identifying the behavioral precursors for wounding and alopecia could allow behavioral managers to implement behavioral interventions before self-wounding or alopecia occurs.

Finally, I reviewed archived behavioral treatment records to determine what impact commonly-implemented treatments at YNPRC had on abnormal behaviors and alopecia in this population. Specifically, I hoped to determine whether certain treatments were more or less effective for different topographies of abnormal behavior. Combined, this information would allow behavioral managers to better identify and treat animals of concern and would also allow limited resources to be directed in a more effective manner.

These analyses tested four basic hypotheses: 1. The types and pattern of abnormal behaviors displayed by rhesus macaques at YNPRC who self-wound differed from behaviors displayed by non-wounders, and the identification of these behavioral predictors could be used to refine the current behavior management system at YNPRC to better identify these animals before they self-injure 2. The types and pattern of abnormal behaviors displayed by animals with alopecia differed from those displayed by animals without significant hair loss 3. The type of treatments included in an animal's behavior management plan were predictive of whether or not that animal was likely to respond to treatment as measured by a reduction in abnormal behavior. 4. The type of treatments included in an animal's behavior management plan were predictive of whether or not the hair coat of animals with alopecia improved with treatment.

CHAPTER 2: GENERAL METHOD

Subjects

The initial subject pool for these analyses consisted of all rhesus macaques housed at the YNPRC main center facility between 2006 and 2014 (*N* = 4615). During the period in which the behavioral data for this study were collected, the animals were housed indoors in cages appropriate to their size and weight (National Resarch Council, 2011). All monkeys received a nutritionally balanced commercial diet supplemented with fresh produce and had ad libitum access to water. In addition, all animals in the colony received enrichment according to standard operating procedures. The level of enrichment at YNPRC has increased over the years, but during the study period, all animals received, at minimum, a perch bar in their home cage, one enrichment toy in the cage, and supplemental produce and foraging mixtures multiple times each week. The YNPRC is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). All research was conducted with approval from Emory University's Institutional Animal Care and Use Committee (IACUC).

Data Collection

Data used for this study were collected as part of a quantitative data collection and management system implemented in August, 2006 by the Behavior Management Unit (BMU). The BMU monitors and enhances the wellbeing of the primates at YNPRC through techniques such as environmental enrichment, socialization, and animal training. The data collection and management program includes frequent behavioral monitoring and documentation by behavior management specialists using a standard, facility-wide ethogram. Trained personnel observe animals in each room of the facility at least three times a week and record the occurrence of any abnormal behavior (see Appendix) using a one-zero sampling technique. Personnel are trained to be a neutral presence in the room and to allow the animals to acclimate to the observer's presence for several minutes before beginning data collection. These observations are performed as part of the behavioral management specialist's daily room walk-throughs. As such, the time spent in each room varies depending on a variety of factors. An informal survey of personnel found that the average time spent in each room was 10 minutes. Personnel are trained on the behavioral ethogram, and periodic inter-observer reliability checks are performed. Observers must achieve 85% agreement on all target behaviors in order to be considered a reliable observer.

These data are entered into an electronic database that allows the behavioral management specialist to summarize and monitor the behavioral data for each animal in the colony. The one-zero data are summarized weekly as the percentage of observations in which each behavior was observed. If abnormal behaviors are observed that exceed predetermined threshold levels, additional evaluations are conducted. These additional evaluations are conducted by performing a series of 5-minute, focal-animal observations using a continuous data collection procedure on a handheld device running Noldus's Observer© software. The focal-animal data includes duration measures for abnormal behaviors as well as social behaviors, enrichment use, and general behaviors such as moving, eating, and vocalizing. If abnormal behavior levels exceed predetermined threshold levels, a behavioral treatment plan is developed, and the animal's response to treatment is monitored.

Our management system includes multiple levels of care depending on the severity and frequency of the abnormal behaviors. Animals placed in our highest level of care (Level 1) receive multi-faceted treatment plans, and focal-animal observations are conducted at least twice monthly to monitor the animal's response to treatment. Elements of an individual animal's treatment plan may include things such as increased foraging opportunities; the addition of enrichment devices such as puzzle feeders, toys, or mirrors; human interaction or training, and housing changes. Animals displaying less severe or less frequent abnormal behaviors are placed in levels of care that require less frequent focal-animal observations and less complex behavioral interventions. All animals continue to be monitored via the three-times-weekly, one-zero data, and all animals receive environmental enrichment according to YNPRC standard operating procedures.

In addition to behavioral data, the BMU also collects data on alopecia and wounds. The hair coat of each animal at the main center facility is periodically assessed. (Assessments were performed biannually from 2007 – 2012 and quarterly thereafter). Personnel must achieve 85% inter-observer reliability on a 4-point system prior to being approved to conduct hair scores. The hair scores reflect the amount of hair coverage on the animal ("1" = 0–25%, "2" = 26–50%, "3" = 51–75%, "4" = 76-100% hair coverage). To more accurately categorize the degree of hair loss, diagrams that break down body areas into approximate percentages are supplied to personnel, and personnel can sketch and describe the pattern of hair loss on these forms. In addition, hair assessments are conducted any time a behavior management specialist notices significant hair loss or gain in an animal.

Hair scores are entered into the electronic database that contains the animals' behavioral data. Animals with less than 76% of the normal hair coverage are evaluated and placed into an appropriate treatment level similar to that described for abnormal behavior. Once again, the level of care depends on the severity of hair loss. Animals with 50% or less of their hair coat are placed in our highest level of care and receive twice-monthly focal-animal behavioral observations and multi-faceted treatment plans to address the alopecia. Hair scores are conducted on these animals at least once every two months. Animals with less severe hair loss are assessed quarterly and also receive an appropriate treatment plan.

Wounding data are collected in accordance with the "Self-Injurious Behavior Scale" developed by the Behavior Management Consortium of all of the National Primate Centers. If a behavior management specialist sees a wound on an animal, a wound score from 1 – 3 is given. On this scale, minor wounds and scratches not requiring medical treatment are scored a 1, moderate wounds requiring veterinary assessment are scored a 2, and severe wounds requiring significant veterinary treatment such as suturing are scored a 3. The wound is further classified by whether it was determined to be self-inflicted (such as a result of self-biting) or from a different or unknown cause (such as a scratch obtained during a social introduction). The wounding score and information about the wounding incident are also entered into the electronic database that houses the animal's behavioral data.

All animals receiving treatment for abnormal behaviors or alopecia are periodically reassessed, and their treatment plans are adjusted accordingly. During this reassessment, the animal's scan-sample and focal-animal data are summarized graphically and statistically. This reassessment period ranges from every 2 months for animals in our highest level of care to "as-needed" for animals with maintenance treatment plans. Any animal evaluated in this system has an electronic folder on the BMU shared directory that contains all of the animal's behavioral data, including scan-sample data, focal-animal data, and scanned copies of any hair score diagrams or wounding reports.

The archival analyses in this study used one-zero behavioral data, treatment records, alopecia scoring, and wounding records collected by BMU personnel. Because focal-animal observations were only conducted on animals already exhibiting abnormal behavior problems, there were not enough subjects with baseline or pre-incident focal-animal observation to include these data in the analyses.

The initial summarization of the data included the dates in which behavioral data were available, whether or not each animal exhibited each topography of abnormal behavior (see Appendix), the presence of any self-inflicted wounds, the lowest hair score recorded for the animal, and the types of treatments provided to each animal. Treatments considered for inclusion in the analyses included 1) additional foraging opportunities (e.g., seed, cereal or other forage provided on a forage board at frequencies above that provided as standard enrichment), 2) the provision of feeding enrichment devices requiring the monkey to manipulate the device to remove food items (e.g., "puzzle feeders" such as challenger balls or peanut feeders), 3) the addition of non-food enrichment items (e.g., toys that hang on the outside of the cage, mirrors, and wood blocks), 4) destructible enrichment (e.g., paper or cardboard distributed once or twice daily), 5) the addition of a visual barrier or privacy panel, 6) housing or socialization changes, 7) human interaction and training, 8) operational changes (e.g., changing cage wash procedures for fearful animals), 9) removal from a research protocol (which may reduce the need for frequent veterinary procedures, enable socialization, or remove other restrictions on the monkey), and 10) pharmacological interventions.

Subjects for each analysis were selected from this initial summary, and additional summaries were prepared for each analysis. In addition to behavioral and treatment data, census data that included the animal’s species, sex, date of birth, and housing information were also used.

Data Analysis

As part of an official accommodation, portions of the data summary process were completed by an undergraduate student funded by the Georgia Tech Office of Disability Services. The student assistant’s tasks included reviewing animal records and summarizing behavioral and treatment data into summary spreadsheets. I (Allison L. Martin) supervised and reviewed these summaries, and I conducted all data analyses, interpretation, and write-up. The statistical packages of IBM SPSS$^{©}$ version 22 and SAS$^{©}$ version 9.4 were used to carry out statistical analyses.

CHAPTER 3

ANALYSIS 1: BEHAVIORAL PREDICTORS OF SELF-WOUNDING

I had two main goals for this analysis. The first was to determine whether there are any behavioral predictors of self-wounding present in rhesus macaques at YNPRC. The second goal was to evaluate and refine the current behavioral evaluation criteria used at YNPRC to identify at-risk animals in this population.

The current behavioral monitoring system at YNPRC includes three classes of behaviors, each with pre-determined thresholds that trigger a behavioral evaluation. An animal exhibiting any SIB resulting in wounding ("class 1" behavior) is immediately placed into the highest level of care. The remaining behaviors are divided into two classes. The second class of behaviors ("class 2") includes persistent fear, self-biting or other SIB not resulting in wounding, and behaviors found in the literature to be correlated with self-wounding or SIB, including hair plucking, floating limb, bizarre posture, self-directed stereotypies, self-directed eye behaviors, digit sucking, and bizarre posture. The third class ("class 3") includes other abnormal topographies such as stereotypic locomotor behaviors, urophagy, fecal behaviors, and regurgitate/reingest (see Appendix).

The threshold for behavioral evaluation is lower for class 2 behaviors than for class 3 behaviors. For example, an animal exhibiting digit-sucking in 50% of observations over a two week period would be evaluated whereas an animal exhibiting stereotypic locomotor behavior would not reach the threshold for evaluation unless that behavior was seen in 80% of observations over a two-week period. While the classification of behaviors into class 2 and class 3 behaviors was based on previous findings (e.g., Bentson et al., 2010; Gottlieb et al., 2013; Lutz et al., 2003; Rommeck et al., 2009), the actual thresholds for evaluation were determined rather arbitrarily. By analyzing the behavioral pre-cursors for self-wounding in this population, I hoped to be able to refine these thresholds to better identify and treat animals prior to a wounding incident.

Method

Subjects

Subject selection and matching.

This analysis involved a matched experimental design where each case animal (those with a history of self-wounding) was matched with a control animal on sex, age, rearing, and single-housing history. Since these factors have previously been found to correlate with an increased risk of SIB, the matched design allowed for control for these variables and concentration on the behavioral predictors of self-wounding.

Subjects included 72 case animals and 72 matched-controls for a total sample of 144 rhesus macaques. To be included in this archival analysis, case animals had to have a history of self-wounding and had to have a minimum of 1 year of behavioral data recorded prior to the first recorded instance of self-wounding. Control animals had to have no history of self-wounding and have behavioral data from the same time period as the case animal. Census records that did not include behavioral history were used for the matching process.

Sex.

Animals were matched categorically by male / female.

Age.

Control animals were matched within 20% of a case animal’s age in days at the time of the first wound. Using a percentage rather than a fixed age criterion allowed for a closer match for younger animals during developmental periods in which age differences may result in meaningful behavioral differences. For example, the control for a 2 year-old case monkey would have to be within 5 months of the case animal’s age. In comparison, the control for a 12 year-old monkey only needed to be within 2.4 years of the case animal.

Using the absolute values of age differences, the average difference between case and control animals was 107 days (*SD* = 160 days, range = 0 – 783 days). The average percent difference for age was 4.0% (*SD* = 4.6%, range = 0 – 19%). For sub-adults (age 5 years and under, *n* = 36 pairs), the average difference in age between case and control animals was 57 days (*SD* = 53 days) whereas for adults, the average difference in age between case and control animals was 158 days (*SD* = 209 days).

Rearing.

Animals were classified as mother-reared, nursery-reared, or transfer animals. Mother-reared animals were born at YNPRC and lived with their birth mother for at least 6 months. Nursery-reared animals were born at YNPRC but were separated from their mother within the first 2 months of their life (actual range was 0 – 36 days). Animals were classified as transfer animals if they transferred from an outside facility from which rearing information was unavailable. Transfer animals were only included if a match could be found who arrived from the same facility on the same date. While not a guarantee, it is likely the animals sent in the same shipment had similar histories.

Single Housing.

The cumulative amount of time that case/control animals were singly housed was matched within 20% as of the date of the case animal's first wound. Again, using a percentage meant that younger animals had to be more closely matched than mature animals. The average absolute value of the difference in single housing between each case and control animal was 132 days (*SD* = 162, range = 0 – 818). That represented an average percent difference in lifetime spent in single housing of 4.6% (*SD* = 4.2%, range = 0 – 18%). Consistent with *The Guide* (National Research Council of the National Academies, 2011), animals housed in panel housing that allowed for only limited social contact with a partner were considered singly housed for this analysis.

While not used as matching criteria, I also assessed differences in the age when first singly housed between case and control animals. Single housing at a young age has also been shown to correlate with SIB (Lutz et al., 2003). The average absolute value in the difference in age first singly housed (even for short periods of time) was 316 days (*SD*= 452 days). There was no significant difference between the average age of first single housing between case (*M* = 774 days, *SD* = 680 days) and control animals (*M* = 732 days, *SD* = 573 days, independent-samples t-test, *t* (141) = 0.41, *p* = .68).

Sample demographics.

Out of the 144 subjects, 116 (81%) were male and 28 (19%) were female. The average age of all subjects was 2700 days or approximately 7.4 years (*SD* = 1455 days). Subjects ranged in age from 751 – 8532 days (2.1 – 23.3 years). The majority of subjects were mother-reared (*n* = 98), followed by nursery-reared (*n* = 24), and transfer animals (*n* = 22). At the time of the first wound, 87.5% of case subjects were singly housed, with the remainder in pair housing. Across all subjects, the average number of days spent singly housed prior to the date of case animal's first wound was 1222 days (3.3 years, *SD* = 1181 days). Days singly housed ranged from 0 – 6953 days (0 - 19 years). This represented an average of 40.4% of the monkey's lifetime spent singly housed (*SD* = 19%, range = 0 – 85%).

Among case animals (*n* = 72), there was no significant difference between males and females for age at first wound (independent samples t-test, *t* (70) = -.94, *p* = .35) or percentage of life singly housed (*t* (70) = 1.37, *p* = .17). The distribution of sexes did differ significantly across rearing histories (Pearson chi-square test, χ^2 (*df* = 2) = 10.11, *p* < .006), with more females (43%) than males (10%) being nursery-reared. In addition, all of the transfer animals were male. Neither the age at first wound (one-way analysis of variance, *F* (2, 71) = 1.75, *p* = .18) nor the percentage of life singly housed (*F* (2, 71) = .5, *p* = .61) differed significantly among rearing histories.

Data Analysis

Behavioral predictors.

Data for this analysis consisted of one-zero behavioral data collected by BMU staff in which the presence/absence of 13 topographies of abnormal behaviors (see Appendix) was noted for each animal during each observation. The observations conducted during the one-year period prior to the case animal's first wounding incident served as the data set for the case animals. The control animals' behavioral data from that same time period served as the data set for the control animals. Observations were conducted a minimum of three times weekly in each room at the YNPRC main center, but the actual number of observations per animal varied as some animals were frequently out of their home cages for testing or other procedures, and observations were sometimes conducted more than three times weekly. The mean number of observations per animal during the one-year period was 175.5 observations (*SD* = 22.7, range 112 - 225). The number of observations did not differ significantly between case and control animals, *t* (142) = -.90, *p* = .37.

These data were summarized as both yes/no data indicating whether or not the behavior was seen during the year preceding the case animal's wound and also as percentage of observations in which the behavior was observed over that year. However, given the low overall incidence of many of the behavioral topographies, I elected to only use the yes/no summaries for further analysis.

The relationship between the 13 individual abnormal behavior topographies and wounding status was examined using Mantel-Haenszel Chi-Square (χ_{MH}) tests for association and Mantel-Haenszel odds ratios (MOR). The Mantel-Haenszel chi-square statistic tests the null hypothesis that after controlling for pair, there is no association between the presence of a behavioral topography and case/control status. The MOR is an odds ratio statistic that adjusts for the matched variables (Kleinbaum & Klein, 2002). In the case of zero cells, a logit estimator was calculated using a correction in which 0.5 monkey was added to each cell in the contingency table, thus allowing an estimation of the odds ratio.

The behavioral topographies were then input as predictor variables into a conditional logistic regression model. Logistic regression is commonly used in epidemiologic data to analyze the impact of risk factors on a dichotomous outcome such as disease/no disease. The conditional logistic regression model allows for a stratified analysis. While it was originally designed for follow-up studies, it is also appropriate for matched (case/control) data (Kleinbaum & Klein, 2002). For this analysis, the outcome measure was whether or not the animal had a history of self-wounding (i.e. whether the animal was a case or control animal). The independent variables were the presence/absence of each behavioral topography during the one-year time period preceding the case animal's first wound, and the strata consisted of the 72 matched pairs. Alpha was set at .05.

To test for multicollinearity, tetrachoric correlations (Ekstrom, 2008; Pearson, 1990) were calculated between the binary predictor variables. Multicollinearity can cause unstable estimates and inaccurate variances. It occurs when one or more of the independent variables can be approximately determined by some combination of the other independent variables (Kleinbaum & Klein, 2002). If the bivariate correlations between variables are high (e.g., > .8), this can indicate the presence of multicollinearity (Midi, Sarkar, & Rana, 2010). Even if no pair of variables is highly correlated, it is still possible that the model includes several interdependent variables (Allison, 2012). Therefore, tolerance and variance inflation factors (VIF) were also calculated. Tolerance and VIF are measures of multicollinearity based on the amount of variance accounted for when each independent variable are regressed on all other independent variables (Midi et al., 2010). Low tolerances (below .4) and high VIF (above 2.5) indicate high multicollinearity (Allison, 2012). While developed for linear models, the VIF has also been shown to be accurate for binary variables in a logistic regression model (Hsieh, Bloch, & Larson, 1998).

Finally, a principal component analysis was run to further examine the relationship between the predictor variables. Principal component analysis is a variable reduction procedure useful if some variables may be redundant or correlated. If redundancy is found, the predictors can be expressed as a smaller number of principal components (O'Rourke & Hatcher, 2013). Because the predictor variables in this model were binary, the principal component analysis was calculated from the tetrachoric correlation matrix. The number of components to retain was based on a bootstrapped version of Horn’s (1965) parallel analysis criteria (Buja & Eyuboglu, 1992) in which the eigenvalues from the original data set were compared with mean eigenvalues computed from 100 random re-samplings of the original data. Only components with eigenvalues greater than the corresponding, mean, bootstrapped eigenvalues were retained.

Number of abnormal behavior topographies.

A separate conditional logistic regression was run in which the independent variable was the number of behavioral topographies displayed by each animal in the one-year period. As in the above analysis, the outcome variable was wounding status, and the strata were the 72 matched pairs.

Alopecia.

To examine the relationship between hair loss and self-wounding, the lowest hair score recorded for each animal during the year prior to the case animal’s first wound was used as the independent variable in a conditional logistic regression model. As described previously, hair scores range from 1 – 4, with 4 indicating a relatively full hair coat. The outcome variable was wounding status, and the 72 matched-pairs were the strata.

Behavioral monitoring assessment.

As discussed previously, the current behavioral monitoring system at YNPRC classifies abnormal behaviors into two classes: class 2 behaviors (SIB or SIB precursors) and class 3 behaviors (other abnormal topographies). In this system, behavioral evaluations are conducted based on different criteria for each class, with lower levels of class 2 behaviors triggering evaluations as compared with class 3 behaviors.

To determine the effectiveness of this behavioral monitoring system in accurately identifying case animals for behavioral evaluation prior to their first wound, two types of analyses were conducted. First, to determine whether the current categorization of behaviors (i.e., class 2 or class 3) appropriately predicted future wounding, two conditional logistic regressions were run in which the independent variables were the presence or absence of behaviors that fell into the two behavioral classes. These models examined whether or not exhibiting a class 2 behavior (SIB or SIB precursors) or class 3 behaviors (other abnormal topographies) predicted whether or not the animal would subsequently self-wound (i.e., be classified as a case animal).

Next, the number of animals identified for behavioral evaluation prior to the case animal's first wound using the existing system was calculated for both case and control animals. Then, new criteria based on the results of the current analyses were retroactively applied to the lifetime behavioral records of each case and control animal, and the results were compared. The goal was to develop criteria that increased the number of case animals identified for behavioral evaluation prior to their first wound.

Results

Behavioral Predictors

Mantel-Haenszel Chi Square tests of association identified statistically significant associations between self-wounding and the behavioral topographies of hair plucking (MOR = 2.5), self-biting (MOR = 23.0), floating limb (logit estimated MOR = 9.0), and digit-sucking (MOR = 9.0, see Table 1). The association between the other behavioral topographies and wounding did not reach statistical significance.

Table 1. Summary of Mantel-Haenszel (MH) Chi-Square Tests and Odds Ratios for Behavioral Predictors of Wounding

Behavior	**# Animals displaying behavior**	**MH Chi-Square**	**sig.**	**MH Odds Ratio**	**95% CI**	
Hair plucking*	27	3.86	0.05	2.50	0.97	6.44
Self-biting*	38	20.17	<.01	23.00	3.11	170.31
Eye behaviors	20	0.00	1.00	1.00	0.38	2.66
Floating limb*	9	7.00	0.01	9.00†	1.63†	49.80†
Other SIB	3	3.00	0.08	0.11†	0.01†	1.51†
Fecal behaviors	21	0.11	0.74	0.80	0.21	2.98
Urine drinking	13	1.00	0.32	2.00	0.50	8.00
Regurgitate/reingest	5	0.20	0.65	1.50	0.25	8.98
Bizarre posture	3	3.00	0.08	0.11†	0.01†	1.51†
Stereotypic locomotor behaviors	100	2.00	0.16	2.00	0.75	5.33
Self-directed stereotypies	33	2.13	0.14	1.88	0.80	4.42
Self-oral*	20	6.40	0.01	9.00	1.14	71.04
Fear	18	0.00	1.00	1.00	0.32	3.10

N = 144

* significant at p = .05 level

† logit estimate used

The full conditional logistic regression model was unable to converge due to the low number of animals exhibiting some topographies of behavior. Therefore, bizarre posture (*n* = 3 subjects displaying this behavior), other SIB (*n* = 3), regurgitate/reingest (*n* = 5), and floating limb (*n* = 9) were excluded from the model. The conditional logistic regression containing the remaining behavioral topographies as predictor variables and wounding status as the outcome variable was significant, χ^2 ($df = 9$) = 30.0, $p < .001$. Of the remaining behavioral topographies, hair plucking and self-biting were the only significant predictors of wounding (see Table 2). None of the bivariate tetrachoric correlations was above .8 (Table 3), all tolerance values were greater than .4, and all VIFs were less than 2.5 (Table 2), indicating that multicollinearity was not a major concern within this model.

Principal component analysis of the tetrachoric correlation matrix was conducted, and the resulting eigenvalues were compared to the corresponding, mean eigenvalues computed in a bootstrapped parallel analysis (Figure 1). This resulted in the retention of one component, with self-biting, self-oral behavior, and stereotypic locomotor behavior all loading heavily (>.7) and self-directed stereotypies loading moderately (>.5) on this component (Table 4).

Table 2. Behavioral Predictors of Wounding: Conditional Logistic Regression Summary, Tolerance (“Tol.”), and Variance Inflation Factor (“VIF”).

Behavior	B	S.E.	Wald	sig.	Exp(B)	95% CI		Tol.	VIF
HPS	2.85	1.22	5.47	.019	17.29	1.59	188.62	.92	1.08
BTE	4.34	1.46	8.79	.003	76.80	4.36	1354.57	.78	1.28
EYE	-0.86	.88	0.96	.328	.43	0.08	2.36	.93	1.08
FEC	-0.98	1.35	0.52	.470	.38	0.03	5.33	.88	1.14
URI	1.17	1.39	0.71	.398	3.221	0.21	48.61	.93	1.08
SLO	0.19	0.67	.08	.781	1.21	0.32	4.52	.89	1.13
SSY	0.01	0.71	0.00	.989	1.01	0.25	4.02	.82	1.22
ORAL	4.97	3.14	2.50	.114	143.93	0.30	68038.12	.76	1.31
FEAR	0.51	0.98	0.27	.602	1.67	0.25	11.35	.92	1.09

Note: See Appendix for behavioral abbreviations

Table 3. Tetrachoric Correlation Matrix for Behavioral Predictors of Wounding

	HPS	**BTE**	**EYE**	**FEC**	**URI**	**SLO**	**SSY**	**ORAL**	**FEAR**
HPS	-	0.14	0.03	0.11	0.22	0.25	0.15	-0.23	0.29
BTE	0.14	-	0.16	0.21	0.30	0.43	0.56	0.54	0.03
EYE	0.03	0.16	-	0.14	0.34	0.20	0.31	0.27	-0.28
FEC	0.11	0.21	0.14	-	0.32	0.33	-0.08	0.52	0.18
URI	0.22	0.30	0.34	0.32	-	0.27	0.00	0.04	0.07
SLO	0.25	0.43	0.20	0.33	0.27	-	0.36	0.56	0.05
SSY	0.15	0.56	0.31	-0.08	0.00	0.36	-	0.31	-0.27
ORAL	-0.23	0.54	0.27	0.52	0.04	0.56	0.31	-	0.32
FEAR	0.29	0.03	-0.28	0.18	0.07	0.05	-0.27	0.32	-

Note: See Appendix for abbreviations

Table 4. Principal Component Analysis Factor Loadings for Variables in the Behavioral Predictors of Wounding Data Set. Factor Loadings with Absolute Values > .5 are Bolded.

Behavior	**Factor Loading**	**Variance Explained**
Hair plucking	0.23	0.05
Self-bite	**0.84**	0.70
Eye	0.41	0.17
Fecal behaviors	0.48	0.23
Urophagy	0.45	0.20
Stereotypic locomotor behavior	**0.72**	0.51
Self-directed stereotypies	**0.55**	0.31
Self-oral behaviors	**0.76**	0.58
Fear	0.15	0.02

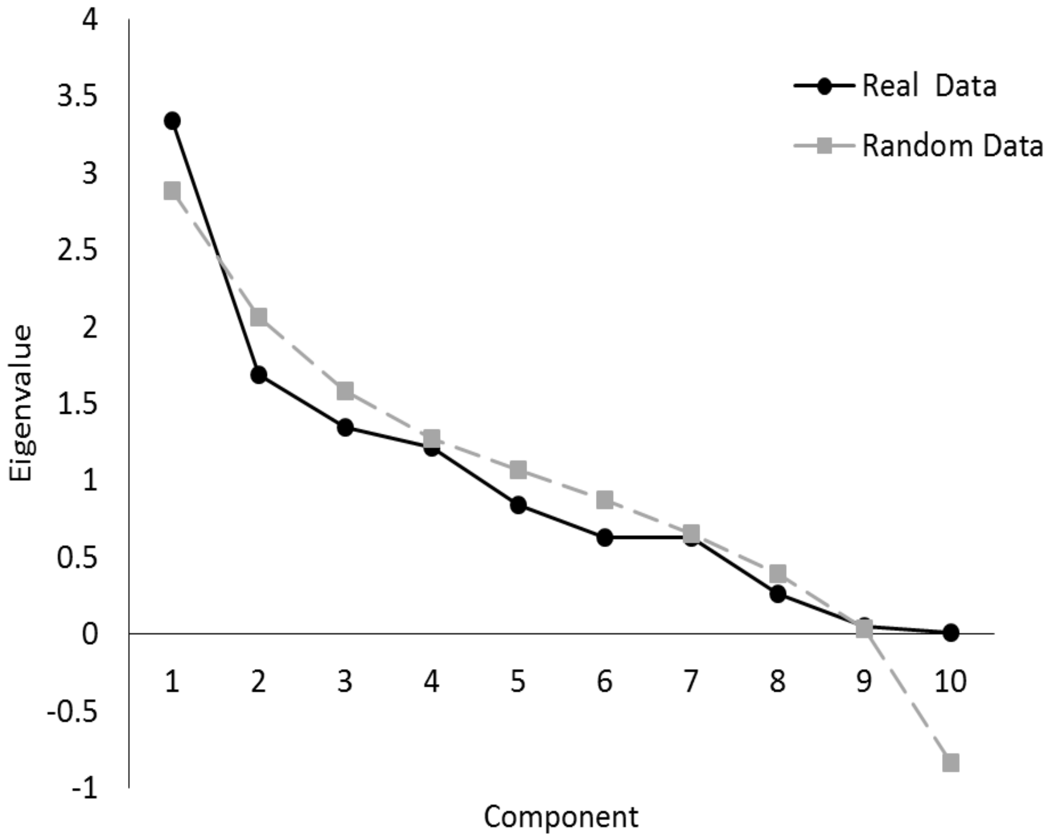

Figure 1. Scree plot showing the eigenvalues for each principal component extracted from the correlation matrix for the behavioral predictors of wounding data set (“Real Data,” Table 3) and the mean eigenvalues of the bootstrapped parallel analysis (“Random Data”).

Number of Abnormal Behavior Topographies

A conditional logistic regression with wounding status as the outcome measure and number of abnormal behavior topographies as the predictor variable resulted in a significant chi-square statistic for overall model fit (χ^2 (*df* = 1) = 15.22, *p* < .001). The number of abnormal topographies of behavior was a significant predictor of wounding status (Wald χ^2 (*df* = 1) = 11.67, *p* = .001). Animals with higher numbers of abnormal behavior topographies were more likely to self-wound (odds ratio/Exp(B) = 2.09, 95% CI [1.37 - 3.18]).

Alopecia

A conditional logistic regression model with wounding status as the outcome measure and hair score (1 – 4) as the predictor variable was not significant (χ^2 (*df* = 1) = <.01, *p* = 1.0). There was no association between low hair score in the previous year and wounding status (odds ratio/Exp(B) = 1.0, 95% CI [0.25 - 4.00]).

Behavioral Monitoring Assessment

Two conditional logistic regression models with wounding status as the outcome measure were run to assess the effectiveness of the current classification of behavioral topographies used by YNPRC. In the first, the presence of any class 2 behaviors (Yes/No) was the predictor variable. For the second model, the presence of any class 3 behaviors (Yes/No) was the predictor. The model with class 2 behaviors was significant for overall model fit (χ^2 (*df* = 1) = 8.17, *p* = .004) with the presence of class 2 behaviors serving as a significant predictor of wounding status (Wald χ^2 (*df* = 1) = 7.06, *p* = .008). Animals who had at least one class 2 behavior were more likely to self-wound (odds ratio/Exp(B) = 3.80, 95% CI [1.42 – 10.18]). In contrast, the model with class 3 behaviors as the predictor variable was not significant (χ^2 (*df* = 1) = 1.0, *p* = .32), with no association between the presence of class 3 behaviors and wounding status (Wald χ^2 (*df* = 1) = .98, *p* = .32, odds ratio/Exp(B) = 1.67, 95% CI [.61 – 4.59]).

Using existing criteria, only 42% of case animals had been evaluated for behavioral issues prior to their first wound. During that same time period, 11% of control animals were evaluated for abnormal behaviors. If the criteria were changed based on the above analyses such that any animal displaying hair plucking or self-biting behavior was evaluated, 65% of case animals and 33% of control animals would have been evaluated prior to the case animal's first wound. If floating limb and self-oral behaviors were also added to the evaluation criteria, 75% of the case animals and 39% of control animals would have met criteria for evaluation in that same time period. Alternatively, the criteria could be based on the number of abnormal behavior topographies. If the criteria were changed such that any animal with two or more topographies of abnormal behavior was evaluated, 67% of case animals and 47% of control animals would have been evaluated in the time period prior to the case animal's first wound.

Discussion

Taken together, results of the Mantel-Haenszel chi square tests and conditional logistic regression provide strong evidence that self-biting and hair plucking are behavioral predictors of self-wounding in rhesus macaques. While not all instances of self-biting result in a wound (Lutz et al., 2003; Reinhardt & Rossell, 2001), it is certainly not surprising that any occurrence of self-biting is predictive of subsequent self-wounding. The relationship between hair plucking and self-wounding is not as well established in the literature, but hair pulling was included in the self-directed stereotypy category found to correlate with self-wounding in the Lutz et al. (2003) study. Additionally, some animals will pluck their hair in a manner that actually causes small wounds to the skin.

Due to the low number of animals (*n* = 9) displaying floating limb behavior during the study period, I was not able to include this behavior as part of the conditional logistic regression model. However, the Mantel-Haenszel Chi Square test did show a significant relationship between floating limb behavior and self-wounding. That, combined with previous studies that describe a correlation between floating limb and self-biting (Bentson et al., 2010; Rommeck et al., 2009) provides evidence that there is a relationship between floating limb and self-wounding.

The relationship between self-oral behavior and wounding was significant when examined individually using the Mantel-Haenszel Chi-Square Test, but it did not retain its significance in the full conditional logistic regression model. Despite tests showing no substantial multicollinearity in the overall model, the confidence interval for the odds ratio for self-oral behavior was extremely wide (Table 2). This may indicate the presence of some multicollinearity (Midi et al., 2010), and subsequent principal component analysis did result in the retention of one dominant component. That component accounted for 58% of the variance in self-oral behavior (Table 4), and the tetrachoric correlation matrix (Table 3) shows moderate correlations between self-oral behaviors and self-biting, fecal behaviors, and stereotypic locomotor behaviors. The relationships between these variables may explain why self-oral was not significant in the full model.

Self-oral behavior is associated with nursery-rearing (Berkson, 1968), and the majority of animals who displayed self-oral behavior in the YNPRC sample were nursery-reared (14/20 were nursery-reared, 4 were mother-reared, 2 were transfer animals). However, it appears that even when rearing is controlled for through the matched design, self-oral behavior may be predictive of subsequent self-wounding. This would also be consistent with the previous findings by Lutz et al. (2003) in which self-directed stereotypic behaviors, which included digit-sucking, were found to be associated with self-wounding.

Previous studies that showed a relationship between stereotypic locomotor behavior and self-injurious behavior differed as to their operational definition of self-injurious behavior. Gottlieb et al. (2013) looked only at self-biting (with or without wounding), and Rommeck et al.'s (2009) dependent measure was self-abuse, which included both non-injurious self-abuse and self-injurious behavior. In both cases, there was a correlation between stereotypic locomotor behavior and self-biting/self-abuse. However, in the Lutz et al. (2003) study, the dependent measure was self-wounding, and no relationship was found between stereotypic locomotor behaviors and this measure. My outcome measure and results are consistent with the Lutz et al. (2003) study, showing no relationship between stereotypic locomotor behaviors and self-wounding in the YNPRC population. Given these varied dependent measures and subsequent results, it may be that stereotypic locomotor behavior is more closely related to non-injurious self-biting than to actual self-wounding. My analysis did show that stereotypic locomotor behavior loaded heavily on the same principal component as self-biting, indicating some comorbidity between stereotypic locomotor behaviors and self-biting in the YNPRC population (Table 4).

A similar pattern was seen with self-directed stereotypies. While I found no relationship between self-directed stereotypies and self-wounding, self-directed stereotypies did load moderately on the same principal component as self-biting (Table 4), indicating some comorbidity. Lutz et al. (2003) found a significant relationship between self-directed behavior and self-wounding in their population. However, the Lutz et al. analysis included a wider range of behaviors in the self-directed behavior category, including hair plucking and self-oral behaviors. The difference in results may be explained by the fact that hair plucking and self-oral behaviors were coded separately in the YNPRC ethogram.

Consistent with findings by Rommeck et al. (2009), there was no relationship found between alopecia and self-wounding in this population. However, only 10/144 animals in this sample showed significant hair loss, limiting the conclusions that can be drawn.

Using existing criteria used by the BMU at YNPRC, less than half of the case animals were identified and evaluated prior to their first wounding event. When the criteria were modified and applied retroactively such that any animal displaying hair plucking, self-biting, floating limb, or self-oral behavior would have been evaluated, the percentage of case animals that would have been evaluated prior to their first wound increased from 42% to 75%. This was the largest percent increase in case animals identified by the three criteria examined. However, because of the personnel time associated with behavioral evaluations, the number of control animals meeting criteria is also important to consider. This criteria also resulted in an increase in control animal evaluations from 11% - 39%. The control animals for this study were matched on risk factors for self-wounding, including single housing and rearing history. Therefore, many of the control animals would also be considered at risk of wounding. Thus, an evaluation rate of 39% in this population may not be unreasonable. The criteria based on number of abnormal behavior topographies was even less efficient, identifying only 67% of case animals while requiring 47% of control animals to be evaluated.

The choice of refined evaluation criteria will require a careful cost/benefit analysis. A recent internal survey of behavioral data from all cage-housed monkeys at

YNPRC found that 39% of animals had displayed two or more topographies of abnormal behavior in their lifetime. This suggests that using the number of abnormal behavior topographies as an evaluation criteria may result in an unreasonably large number of behavioral evaluations. However, relatively few animals exhibited the behavioral topographies of hair plucking (12%), self-biting (8%), self-oral behaviors (7%), and floating limb (3%) in their lifetime, suggesting that criteria based on these topographies of behavior might result in a more reasonable work load for behavioral personnel while maximizing the number of animals properly identified and evaluated prior to a wounding incident.

It is hoped that earlier identification based on these behavioral predictors will allow for interventions that prevent the development of self-wounding in these animals. While there are limited effective treatments for SIB, both socialization (Line et al., 1990; Reinhardt, 1999; Weed et al., 2003) and medications (Fontenot et al., 2005 & 2009; Kempf et al., 2012; Macy et al., 2009; Tiefenbacher et al., 2005; Weld et al., 1998) have been found to reduce SIB in rhesus macaques. Therefore animals displaying behavioral predictors should be prioritized for socialization and considered for drug treatment when warranted.

Additionally, if an animal is identified as being at risk for future self-wounding, an effort could be made to reduce additional risk factors for self-wounding. While ideal practices would allow for mother-rearing for all captive NHP, research and clinical needs still result in the nursery-rearing of some animals in laboratory settings. A behavioral manager cannot undo the effects of nursery-rearing, but if an animal displays behaviors known to predict future self-wounding, care can be taken to reduce additional risk factors of self-wounding including single housing (Gottlieb et al., 2013; Lutz et al., 2003; Rommeck et al., 2009), cage position within the room (Gottlieb et al., 2013), and exposure to stressful events such as relocations (Davenport et al., 2008; Gottlieb et al., 2013; Rommeck et al., 2009) or veterinary procedures (Lutz et al., 2003; Novak, 2003). At-risk animals could be moved to a cage in the top rack and away from the door. When possible, these animals could also be assigned to research protocols that require minimal veterinary procedures or relocations. Early intervention that minimizes additional risk factors may be successful in preventing some wounding incidents.

CHAPTER 4

ANALYSIS 2: BEHAVIORAL PREDICTORS OF ALOPECIA

The aim of this analysis was to determine whether there are any behavioral predictors of alopecia in rhesus macaques at YNPRC. Behavioral data collected from the one-year period prior to the development of alopecia in case animals was compared with behavioral data from control animals matched on factors that have been found to relate to alopecia, such as sex (Kramer et al., 2010; Kroeker et al., 2014; Luchins et al., 2011; Lutz et al., 2013, Steinmetz et al., 2006) and age (Beisner & Isbell, 2009; Huneke, Foltz, VandeWoude, Mandrell, & Garman, 1996; Kramer et al., 2010; Kroeker et al., 2014, Steinmetz et al., 2006). Socially-housed animals were excluded from the study to eliminate the possibility of hair loss caused by over-grooming by social partners. In addition, because pair-housed macaques have been found to exhibit less alopecia than singly-housed macaques (Kroeker et al., 2014), subjects were matched based on the percentage of the previous year spent in single housing.

Method

Subjects

Subject selection and matching.

Similar to Analysis 1, this analysis involved a matched experimental design in which each case animal (animals with hair scores less than 4, indicating hair cover less than or equal to 75% of their body surface) was matched with a control animal (those with a hair score of 4). Subjects included 55 case animals and 55 matched-controls for a total sample of 110 rhesus macaques. To be included in this analysis, all animals had to have been housed in a manner that prohibited grooming contact with another monkey for at least 6 months prior to the date of the first <4 hair score in the case animal. This ensured that the development (or worsening) of alopecia was not due to over-grooming by a social partner. Most animals were housed singly during the one-year study period. Panel-housed monkeys (7.3% of subjects) were included only if the panel size and configuration prevented the possibility of social grooming (e.g., animals housed in cages separated by panels with very small holes and/or double panels that ensured minimal contact). Consistent with *The Guide* (National Resarch Council, 2011), both panel and singly-housed animals were considered singly housed for the remainder of this analysis.

To be included in this archival analysis, case animals had to have a documented hair score below 4 and have a minimum of 1 year of behavioral data recorded prior to the first low hair score. Control animals had to have no history of significant alopecia (defined by a hair score of 4) and had to have behavioral data from the same time period as the case animal. Additionally, because differences in alopecia have been noted between animals housed in indoor as compared with outdoor housing (Steinmetz, Kaumanns, Dix, Neimeier, & Kaup, 2005 & Steinmetz et al., 2006), I limited this sample to animals who had been housed indoors for at least one year prior to the case animal's first < 4 hair score. Census records that did not include behavioral history were used for the matching process.

Sex.

Animals were matched categorically by male / female.

Age.

Control animals were matched within 20% of the case animal's age in days at the time of the first < 4 hair score. Using the absolute values of age differences, the average difference between case and control animals was 159 days (*SD* = 230, range = 2 – 1124 days). The average percent difference for age was 4.4% (*SD* = 5.2%, range = 0.1 – 19.6%).

Housing.

In addition to the requirement that all animals were singly housed for at least six months prior to the development of alopecia in the case animal, case and control animals were also matched on the percentage of the prior year spent singly housed. The average absolute value of the difference in single housing in the year-long study period was 2.2 days (*SD* = 8.2, range = 0 – 47 days). That represented an average percent difference of the prior year spent in single/panel housing of 0.7% (*SD* = 2.4%, range = 0 – 13.6%).

Sample demographics.

There were 58 males (52.7%) and 52 females (47.3%) in this analysis. The average age for subjects was 3307 days or approximately 9.1 years (*SD* = 1685 days, range = 1321 – 7525 days, or 3.6 – 30.6 years). The variances in ages between sexes was not equal (Levene's test, $F = 20.1$, $p < .001$), so a corrected independent samples t-test was run to compare the ages between males and females in this sample. Males in this sample were significantly younger (*M* = 2534 days/6.9 years, *SD* = 1174 days/3.2 years) than females (*M* = 4169 days/11.4 years, *SD* = 1758 days/4.8 years, t (87.4) = -5.78, $p <$ .001).

The majority (80%) of subjects were mother-reared. Transfer animals made up 14.5% of the sample, and 5.5% of subjects were nursery-reared. The distribution of rearing histories did not differ significantly between case and control animals (χ^2 (*df* = 2) = 1.09, *p* = .58) or across sex (χ^2 (*df* = 2) = 1.00, *p* = .61). Subjects were single/panel housed for an average of 34.4% (*SD* = 22.5%, range = 5.9 – 96.6%) of their lifetime. There was no significant difference in percentage of lifetime singly housed between case and control animals (independent samples t-test, *t* (108) = -.38, *p* =.70), nor was there a significant difference in lifetime singly housed between males and females (t (corrected *df* = 93.1) = .29, *p* = .77).

Data Analysis

Data for this analysis consisted of one-zero behavioral data and hair scores collected by BMU staff. For the behavioral predictors, the presence/absence of 13 topographies of abnormal behaviors (see Appendix) was noted for each animal during observations conducted in the year prior to the case animal's first low hair score. For this analysis, subjects averaged 172.8 behavioral observations in the year-long study period (*SD* = 33.5, range = 85 – 232). There was no difference in the number of observations conducted between case and control animals, *t* (108) = .95, *p* = .34. Behavioral data were summarized as yes/no data reflecting whether or not each behavior was seen during the year preceding the case animal's first low hair score.

The remainder of the analyses were identical to those in Analysis 1. The relationship between the 13 individual abnormal behavior topographies and alopecia status was examined using Mantel-Haenszel Chi-Square (χ^2_{MH}) tests for association and Mantel-Haenszel odds ratios (MOR). In the case of zero cells, a logit estimator was calculated using a correction in which 0.5 monkey was added to each cell in the contingency table, thus allowing an estimation of the odds ratio.

The behavioral topographies were then input as predictor variables into a conditional logistic regression model. For this analysis, the outcome measure was whether or not the animal had alopecia (as defined by a hair score < 4). The independent variables were the presence/absence of each behavioral topography during the one-year time period, and the strata consisted of the 55 matched pairs. Alpha was set at .05. To test for multicollinearity, tetrachoric correlations were examined, and tolerance and VIF were calculated for each variable.

Finally, a principal component analysis was calculated from the tetrachoric correlation matrix to further examine the relationship between the predictor variables. The number of components to retain was based on a bootstrapped version of Horn's (1965) parallel analysis criteria (Buja & Eyuboglu, 1992).

Results

No subjects in this analysis displayed behavior categorized as other self-injurious behavior, so that behavior was excluded from analysis. Among the other 12 behaviors, stereotypic locomotor behavior was the most prevalent (seen in 53/110 subjects), followed by hair plucking (*n* = 19), and self-directed stereotypies (*n* = 17, see Table 5). Mantel-Haenszel Chi Square tests of association identified statistically significant associations between alopecia and the behavioral topographies of stereotypic locomotor behavior (MOR = 0.2) and fear (logit estimated MOR = 9.0). The association between the other behavioral topographies and alopecia did not reach statistical significance (see Table 5).

Table 5. Summary of Mantel-Haenszel (MH) Chi-Square Tests and Odds Ratios for Behavioral Predictors of Alopecia

Behavior	**# Animals displaying behavior**	**MH Chi-Square**	**sig.**	**MH Odds Ratio**	**95% CI**	
Hair plucking	19	1.67	0.20	2.00	0.68	5.85
Self-biting	9	1.29	0.26	0.40	0.08	2.06
Eye behaviors	7	1.80	0.18	0.25	0.03	2.24
Floating limb	5	0.20	0.65	0.67	0.11	3.99
Other SIB	0	-	-	-	-	-
Fecal behaviors	11	2.27	0.13	0.38	0.10	1.41
Urine drinking	7	0.14	0.71	0.75	0.17	3.35
Regurgitate/reingest	3	0.33	0.56	2.00	0.18	22.06
Bizarre posture	11	2.27	0.13	2.67	0.71	10.05
Stereotypic locomotor behavior*	53	9.78	< 0.01	0.21	0.07	0.62
Self-directed stereotypies	17	0.11	0.74	1.25	0.34	4.65
Self-oral behaviors	8	0.00	1.00	1.00	0.20	4.95
Fear *	5	5.00	0.03	9.00†	1.19†	68.13†

N = 110

* significant at *p* = .05 level
† logit estimate used

The full conditional logistic regression model was unable to converge due to the low number of animals exhibiting many topographies of abnormal behavior. Therefore, the behavioral predictors of regurgitate/reingest (*n* = 3), floating limb (*n* = 5), fear (*n* = 5), and urine drinking (*n* =7) were excluded from the model. The conditional logistic regression model that included the behavioral predictors of hair plucking, self-biting, fecal behaviors, bizarre posturing, stereotypic locomotor behaviors, and self-directed stereotypies was significant, χ^2 (*df* = 6) = 16.33, *p* = .012. Within this model, only stereotypic locomotor behavior was a significant individual predictor of alopecia status (Wald χ^2 (*df* = 1) = 7.83, *p* = .005). Animals who were observed displaying stereotypic locomotor behaviors were less likely to develop alopecia (odds ratio/Exp(B) = 0.09, 95% CI [0.02 – 0.50]). No other behavioral predictors reached statistical significance (see Table 6).

Table 6. Behavioral Predictors of Alopecia: Conditional Logistic Regression Summary, Tolerance (“Tol.”), and Variance Inflation Factor (“VIF”).

Behavior	**B**	**SE**	**Wald**	**Sig.**	**Exp(B)**	**95% CI**		**Tol.**	**VIF**
HPS	1.70	.93	3.32	.07	5.49	.88	34.25	.86	1.16
BTE	-1.36	1.20	1.27	.26	.26	.02	2.72	.91	1.10
FEC	-.24	.98	.06	.81	.79	.12	5.36	.85	1.17
BIZ	1.42	.99	2.06	.15	4.14	.60	28.81	.97	1.03
SLO	-2.32	.83	7.84	.01	.10	.02	.50	.72	1.40
SSY	.69	.97	.51	.48	2.00	.30	13.39	.82	1.22
ORAL	-.08	1.06	.01	.94	.92	.12	7.34	.85	1.18

Note: See Appendix for behavioral abbreviations

None of the bivariate tetrachoric correlations was above .8 (Table 7), all tolerance values were greater than .4, and all VIFs were less than 2.5 (Table 6), indicating that multicollinearity was not a major issue in this model. The eigenvalues calculated from the tetrachoric correlation matrix were compared with the mean eigenvalues of a bootstrapped parallel analysis (Figure 2). Tetrachoric (or polychoric) correlations frequently produce non-Gramian correlation matrices, and this can produce the unusual eigenvalue pattern seen in Figure 2. No components were retained based on these criteria, further indicating a lack of significant relationships between predictor variables.

Table 7. Tetrachoric Correlation Matrix for Behavioral Predictors of Alopecia

	HPS	**BTE**	**FEC**	**BIZ**	**SLO**	**SSY**	**ORAL**
HPS	-	0.29	0.02	0.20	0.60	0.38	0.34
BTE	0.29	-	0.30	0.30	0.58	0.33	0.40
FEC	0.02	0.30	-	-0.03	0.64	0.06	0.53
BIZ	0.20	0.30	-0.03	-	-0.04	-0.17	0.07
SLO	0.60	0.58	0.64	-0.04	-	0.65	0.55
SSY	0.38	0.33	0.06	-0.17	0.65	-	0.54
ORAL	0.34	0.40	0.53	0.07	0.55	0.54	-

Note: See Appendix for abbreviations

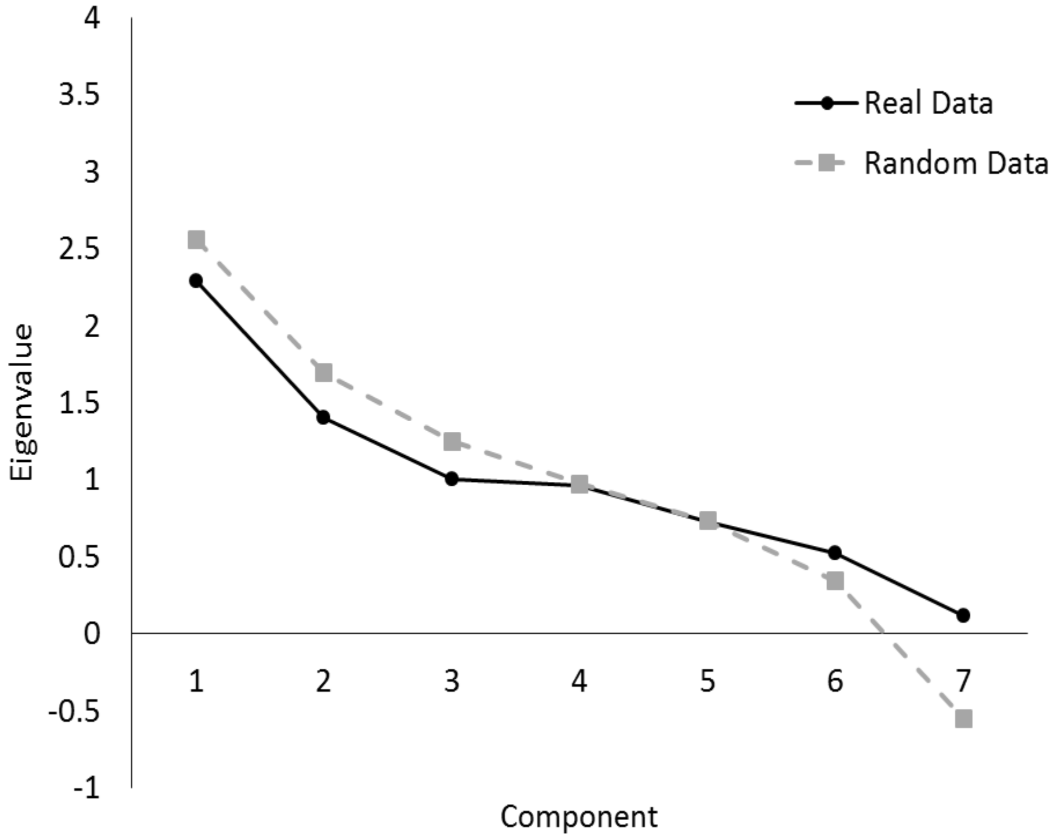

Figure 2. Scree plot showing the eigenvalues for each principal component extracted from the correlation matrix for the behavioral predictors of alopecia data set ("Real Data," Table 7) and the mean eigenvalues of the bootstrapped parallel analysis ("Random Data").

Discussion

Contrary to previous findings (Luchins et al., 2011; Lutz et al., 2013; Martin, Perlman, et al., 2011), hair plucking was not found to be a significant predictor of alopecia in this population. Relatively few case (21.8%) or control (12.7%) animals were observed hair plucking during the one-year study period. It may be that our behavioral sampling techniques failed to identify animals who do actually engage in hair plucking. However, this also supports the idea that alopecia is a condition with a variety of etiologies that include not only behavioral causes such as hair plucking but may also involve factors not accounted for in this analysis, including hormonal and genetic factors, inflammation, parasitic or bacterial infections, and stress (Novak et al., 2014; Novak & Meyer, 2009).

Although very few animals in this sample (5 of 110 subjects) displayed fear behaviors, all of these animals were case animals. While a larger sample size is needed to confirm these findings, this suggests that fear may be a behavioral predictor of alopecia. This would be contrary to the Coleman et al. (2015) findings that animals with anxious or inhibited temperaments were less likely to have alopecia. In the Coleman et al. study (N = 101), a negative correlation was found between alopecia and the time a monkey spent freezing or in the back of its cage during a Human Intruder Test used to assess temperament. The Human Intruder Test involved several phases in which an unfamiliar person entered a room and stared at, stood in profile with, and then stood with his or her back to the animal. The relationship between freezing and alopecia status was observed during the profile period in which the unfamiliar person stood in profile with the animal and avoided direct eye contact. Although the BMU personnel collecting data on the YNPRC monkeys are generally familiar to the animals, the observational procedures (standing to the side and avoiding direct contact) are similar to those in the Colman et al. study, and freezing is also included as a fear behavior in the YNPRC ethogram. The conflicting results could be due to the familiarity of the observer or to facility differences. Coleman et al. did find significant differences in reactions to the Human Intruder test across the four facilities in their study. More research is needed to better understand the relationship between fear and alopecia.

The most prevalent abnormal behavior in this sample was stereotypic locomotor behavior, with 48% of animals displaying this behavior. Case animals (those with significant hair loss) were significantly less likely than control animals to display locomotor stereotypies. Interestingly, the Coleman et al. (2015) study investigating the relationship between temperament and alopecia also found a negative correlation between pacing behavior and alopecia. In humans and nonhuman animals, both stereotypies (Ijichi, Collins, & Elwood, 2013; Mason, 1991b; Mason & Latham, 2004; Soussignan & Koch, 1985) and hair pulling or trichotillomania (Christenson, Mackenzie, & Mitchell, 1991; Miltenberger, 2005) have been suggested as coping mechanisms that function to decrease stress or arousal. From a behavior analytic perspective, this represents an automatic negative reinforcement function whereby the behavior is maintained by the removal of an aversive internal sensation such as tension (Miltenberger, 2005). While more research is needed, it may be that stereotypic locomotor behavior reduces tension that might otherwise lead to hair plucking and/or alopecia in captive primates.

As suggested by Coleman et al. (2015), the pattern of hair loss may be an important factor to consider, and one that was not addressed in this analysis. It may be that animals who hair pluck are more likely to present with small, focal areas of hair loss that do not meet the current YNPRC criteria for alopecia (25% or more hair loss). Kramer, Mansfield, Simmons, and Bernstein (2011) found that animals with alopecia localized on lower limbs did not show any of the skin abnormalities seen in many animals with a more widespread, generalized pattern of alopecia. This suggests that the localized, lower-limb alopecia may be of psychogenic origin. Future refinement of the alopecia scoring system to include these animals may allow for further investigation into the causes of different patterns of alopecia in NHP.

CHAPTER 5

ANALYSIS 3: TREATMENT EFFECTIVENESS IN REDUCING ABNORMAL BEHAVIORS

Three analyses were conducted to investigate the effectiveness of different treatments in reducing abnormal behaviors in rhesus macaques. The first analysis examined the effectiveness of the treatment types on the overall reduction of abnormal behavior. The others focused specifically on the reduction of stereotypic locomotor behavior and self-biting. The behavioral treatments analyzed included additional foraging opportunities (e.g., seed, cereal or other forage provided on a forage board once or twice daily), the provision of feeding enrichment devices requiring the monkey to manipulate the device to remove food items (e.g., “puzzle feeders” such as challenger balls or peanut feeders), the addition of non-food enrichment items (e.g., toys that hang on the outside of the cage, mirrors, and wood blocks), destructible enrichment (e.g., paper or cardboard distributed once or twice daily), and the addition of a visual barrier or privacy panel. Other treatments, including housing or socialization changes, human interaction and training, operational changes, and pharmacological interventions did not have enough subjects to be included in the analysis. In addition, the analysis included the control variables of sex (male/female), age (days at start of treatment), percentage of life spent in single housing at the start of treatment, and rearing history (mother-reared, nursery-reared, or transfer).

Method

Subjects

Subject selection.

The initial subject pool for this archival analysis was any rhesus macaque who underwent treatment for abnormal behavior at YNPRC from 2006 – 2014. To be included in the analysis, subjects had to have two months of behavioral data prior to the start of treatment (baseline period) and had to remain on that treatment with no treatment changes for at least two months (treatment period). Additionally, animals could only be included if they displayed the target abnormal behavior(s) during the two-month baseline period. For example, an animal presenting with a wound suspected to be self-inflicted would be placed into treatment but might not have been observed to self-bite or display any other abnormal behavior during formal behavioral observations. If no abnormal behaviors were noted during baseline behavioral observations, that animal was not included in this analysis.

Sample demographics.

Total abnormal behavior.

The sample for this analysis included 75 male and 25 female rhesus macaques, for a total sample size of $N = 100$. The majority ($n = 61$) were mother-reared, with 23 nursery-reared animals and 16 animals who transferred from an outside facility. The distribution of sexes among rearing types differed significantly (Pearson chi-square, $df = 2$, $\chi^2 = 6.93$, $p = .03$) with a higher proportion of females (40%) than males (17.3%) having been nursery-reared.

The average age at the start of treatment was 2282 days / 6.25 years ($SD = 1350$ days, range = 459 – 8072 days or 1.3 - 22.11 years). There was no significant difference in age at first treatment between male and female subjects (independent samples t-test, *t*

(98) = .13, *p* = .88) or across rearing histories (one-way analysis of variance, *F* (2, 99) = 2.79, *p* = .07). The average percentage of the monkey's lifetime spent in single housing was 43.3% (*SD* = 25.4%, range = 0 – 100%). The variances in the percentage of lifetime spent singly housed were not equal between sexes (Levene's Test, *F* = 12.32, *p* = .001); therefore, a corrected independent samples t-test was used to determine that there was no significant difference between male and female subjects in percentage of the animal's lifetime spent in single housing, *t* (31.2) = -1.89, *p* = .07. Nursery-reared animals spent significantly more of their life in single housing (*M* = 57.9%, *SD* = 30.1%) than mother-reared (*M* = 40%, *SD* = 23.0%) or transfer animals (*M* = 34.4%, *SD* =19.2%, one-way analysis of variance, *F* (2, 99) = 5.74, *p* = .004). However, it is important to note that it is not known whether or not transfer animals were singly housed at their previous facility.

At the time treatment was initiated, 87% of subjects were singly housed. The percentage of animals currently in single or pair housing did not differ across sex (χ^2 (*df* = 1) = .27, *p* = .61) or rearing history (χ^2 (*df* = 2) = 1.04, *p* = .60).

Stereotypic locomotor behavior.

A total of 75 monkeys met criteria for inclusion in the analysis to evaluate the effects of treatment type on stereotypic locomotor behavior. Of these, 78.7% were male (21.3% female), 57.3% were mother-reared, 26.7% were nursery-reared, and 16% transferred from an outside facility. As in the previous analysis, the distribution of male and female animals across rearing types differed significantly (χ^2 = 8.89, *p* = .012), with a greater percentage of female subjects (50%) having a history of nursery-rearing when compared with male subjects (20.3%).

The average age of all subjects was 2306 days/6.32 years (SD = 1329 days, range = 459 – 8072 days or 1.3 – 22.1 years). The average percentage of life spent in single housing was 44.3% (*SD* = 24.6%, range = 0 – 100%). Male and female subjects did not differ significantly on age when treatment began (independent samples t-test, *t* (73) = .51, *p* = .61). The variances of percentage of life spent in single housing differed across sexes (Levene's test, *F* = 9.42, *p* = .003). A t-test taking the unequal variances into account found no significant difference between males and females in the percentage of life spent singly housed, *t* (18.3) = -1.95, *p* = .07.

Both age (one-way analysis of variance, *F* (2, 74) = 4.32, *p* = .017) and percentage of life singly housed (*F* (2, 74) = 6.04, *p* = .004) varied across rearing histories. Mother-reared animals (*M* = 2678 days / 7.3 years, *SD* = 1380 days) were older at the start of treatment than nursery-reared animals (*M* = 1772 days / 4.9 years, *SD* = 1215 days). All three rearing histories differed in percentage of time singly housed, with nursery-reared animals having the highest percentage (*M* = 56.6%, *SD* = 29.4%), followed by mother-reared (*M* = 43.2%, *SD* = 21.3%), and transfer animals (*M* = 27.6%, SD = 15.6%).

At the time treatment was initiated, 89.3% of animals were singly housed and 10.7% were pair housed. Current housing status did not differ significantly across sex (χ^2 (*df* =1) = .42, *p* = .52) or rearing type (χ^2 (*df*=2) = .55, *p* = .76).

Self-biting.

Only 45 subjects qualified for inclusion in this analysis. Of these, 77.8% were male (22.2% female), 48.9% were mother-reared, 35.6% were nursery-reared, and 15.6% transferred from an outside facility. There was no difference in the percentage of male and female animals across rearing histories (Pearson chi-square, χ^2 (*df* = 2) = 4.37, *p* = .11).

The average age at the time of first treatment was 2294 days/ 6.28 years (*SD* = 1408 days / 3.86 years, range = 762 – 7091 days or 2.1 – 19.4 years). Males and females did not differ significantly in age at time of treatment (independent samples t-test, *t* (43) = -.66, *p* = .52). On average, animals in this analysis spent 44.8% of their lives in single housing (*SD* = 23.5%, range = 0.6% - 100%). The variances in percentage of lifetime spent in single housing differed significantly between males and females (Levene's test, *F* = 8.83, *p* = .005); therefore, a corrected t-test was run to determine that the percentage of time spent singly housed also did not differ between the sexes, *t* (10.4) = -.53, *p* = .72. Neither age (one-way analysis of variance, *F* (2, 42) = 1.25, *p* = .30) nor percentage of life singly housed (*F* (2, 42) = 2.00, *p* = .15) differed across rearing histories.

At the time treatment was initiated, 88.9% of monkeys were singly housed (with 11.1% pair housed). The proportion of males and females housed singly at the time of treatment did not differ significantly, χ^2 (*df* = 1) = 1.03, *p* = .31. This distribution of animals single or pair housed also did not differ across rearing histories, χ^2 (*df* = 2) = 1.05, *p* = .59.

Data Analysis

The independent variable for these analyses consisted of whether or not the subject's prescribed treatment plan included each of the five treatment types (additional forage, puzzle feeders, destructible enrichment items, non-food enrichment items, or a visual barrier). Most treatments consisted of multiple treatment types, so the pattern and number of treatments varied across subjects.

The dependent measures differed by analysis but were based on the one-zero behavioral data collected in the two months before (baseline period) and after treatment was initiated (treatment period). The average number of behavioral observations per subject over the total four-month study period was 59.8 (*SD* = 9.0, range = 35 - 88). The number of observations did not differ significantly between the baseline and treatment phases (paired-sample t-test, *t* (99) = .54, *p* = .59).

For total abnormal behaviors, the dependent measure was based on an index calculated by dividing the total number of abnormal behaviors recorded by the number of observations conducted. Once the index was calculated for the baseline and treatment phases, each animal was scored as improved (abnormal behavior index decreased from baseline to treatment) or not-improved (abnormal behavior index increased or stayed the same from baseline to treatment).

For the stereotypic locomotor and self-biting analyses, the dependent measure was based on the percentage of scans in which each behavior was observed. Once again, animals were scored as either improved (the percentage of scans in which stereotypic locomotor or self-biting was observed decreased from baseline to treatment) or not-improved (the percentage of scans in which the behavior was observed increased or stayed the same from baseline to treatment). The other topographies of behavior did not have a sufficient sample size to permit individual analysis.

The treatment analyses did not involve a matched design. Therefore, the following variables were analyzed as control variables: sex (male/female), age (days at start of treatment), percentage of life spent in single housing as of the start of treatment, and rearing history (mother-reared, nursery-reared, or transfer).

The relationship between behavioral improvement and each control and treatment variable was first examined individually using either Pearson chi-square tests (categorical variables) or independent-samples t-tests (continuous variables). The significance level was set at .05 for all tests. Then, treatment and control variables were entered into a main-effects logistic regression model in which the outcome variable was improvement/no improvement. As in previous analyses, multicollinearity was assessed by examination of the correlation matrix and the calculation of tolerance and VIF for each variable. However, because the predictor variables differed by scale of measurement, the correlation matrix consisted of a mixture of Pearson correlations (continuous*continuous variables), polyserial correlations (discrete*continuous variables), and tetrachoric / polychoric correlations (discrete*discrete variables). Principal component analyses were then calculated from the resulting correlation matrix, and a bootstrapped version of Horn's (1965) parallel analysis criteria (Buja & Eyuboglu, 1992) was used to determine retention of components.

Results

Total Abnormal Behavior

There was no significant reduction in the average number of abnormal behaviors per observation between the baseline (*M* = .30, *SD* = .29) and treatment periods (*M* = .30, *SD* = .31, independent samples t-test, *t* (99) = .02, *p* = .98). Overall, 53% of subjects showed improvement in the treatment period while 47% stayed the same or had increased levels of abnormal behavior during the treatment period. In this sample, 81% of subjects received additional forage, 44% received non-food enrichment, 44% received a visual barrier, 31% received destructible enrichment items, and 28% of subjects received a puzzle feeder. The average number of treatment types per subject was 2.28 (*SD* = .95, range 1 – 5). Animals who improved did not differ in number of treatments from those who did not improve (independent samples t-test, *t* (98) = 1.02, *p* = .31).

Animals who did/did not improve did not differ significantly by age (*t* (98) = 1.12, *p* = .27) or percentage of life spent in single housing (*t* (98) = 1.7, *p* = .09). Neither sex (χ^2 (*df* =1) = 0.13, *p* = .91) nor rearing history (χ^2 (*df* = 2) = 1.13, *p* = .57) was predictive of improvement. When examined individually, no treatment type was found to be predictive of improvement status (see Table 8).

Table 8. Summary of Pearson Chi-Square Tests and Odds Ratios for Treatment Type (Additional Forage, Puzzle Feeders, Non-Food Enrichment, Destructible Enrichment, and Visual Barrier) and Improvement of Abnormal Behavior, Stereotypic Locomotor Behavior, and Self-Biting.

		Forage	**Puzzle**	**Non-Food**	**Destruct.**	**Visual Barrier**
Abnormal Total	Chi-Square	0.97	1.99	3.04	0.61	0.88
	sig.	0.32	0.16	0.08	0.81	0.35
	Odds Ratio	0.60	1.90	0.49	1.11	0.69
	95% CI	0.21	0.77	0.22	0.48	0.31
		1.67	4.68	1.10	2.61	1.52
Stereotypic Locomotor Behavior	Chi-Square	0.48	0.53	1.68	0.54	1.11
	sig.	0.49	0.47	0.20	0.46	0.29
	Odds Ratio	1.50	1.45	0.55	1.44	0.61
	95% CI	0.48	0.53	0.22	0.54	0.25
		4.74	3.94	1.37	3.81	1.53
Self-Biting	Chi-Square	0.03	0.19	3.38	0.83	0.01
	sig.	0.87	0.67	0.07	0.36	0.92
	Odds Ratio	0.87	0.73	0.29	0.55	1.07
	95% CI	0.15	0.17	0.08	0.15	0.30
		5.12	3.06	1.12	2.03	3.77

A logistic regression model with improvement (yes/no) as the outcome variable; sex (male/female), age (days), rearing history, and percentage of life spent in single housing as control variables; and additional forage, puzzle feeders, destructible enrichment, non-food enrichment, and visual barrier (yes/no) as the predictor variables was not significant, χ^2 ($df = 9$) = 9.80, $p = .37$. Within the model, only nonfood enrichment had a significant relationship with improvement outcome (Wald χ^2 ($df = 1$) = -.90, $p = .045$). Animals given non-food enrichment were less likely to improve than those not provided with non-food enrichment (odds ratio / exp(B) = .41, 95% CI [.17 - .98]). No other variables reached statistical significance (Table 9). All tolerance levels were above .4, and all VIFs were below 2.5 (Table 9). In addition, no bivariate correlations exceeded .8 (Table 10).

Finally, a principal component analysis was calculated from the mixed (Pearson, polyserial, polychoric, and tetrachoric) correlation matrix. Eigenvalues calculated from these data were compared with the corresponding mean eigenvalues from the bootstrapped parallel analysis, and two components were retained (Figure 3). The retention of these components reflects the presence of inter-dependencies between variables. These dependencies resulted from existing relationships among demographic variables and/or the unequal distribution of treatments. Age at time of treatment, rearing history, additional forage enrichment, and non-food enrichment all loaded moderate/high (absolute value > .5) on the first component. The second component included moderate/high loadings for sex and percentage of time spent in single housing. See Table 11 for factor loadings.

Table 9. Treatment of Abnormal Behavior: Logistic Regression Summary, Tolerance ("Tol."), and Variance Inflation Factor ("VIF").

Variable	**B**	**SE**	**Wald**	**sig.**	**Exp(B)**	**95% CI**		**Tol.**	**VIF**
Sex	.18	.53	.12	.73	1.20	.43	3.39	.86	1.17
Age	<.01	<.01	.58	.45	1.00	1.00	1.00	.85	1.18
Rearing	-.09	.30	.08	.78	.92	.51	1.65	.87	1.15
Single Housing	-.01	.01	1.50	.22	.99	.97	1.01	.81	1.23
Puzzle	.43	.49	.77	.38	1.53	.59	3.99	.93	1.07
Forage	-.49	.58	.72	.40	.61	.20	1.91	.89	1.12
Visual barrier	-.27	.45	.38	.54	.76	.32	1.82	.90	1.11
Destructible	.02	.48	<.01	.97	1.02	.40	2.60	.92	1.09
Non-food	-.90	.45	4.03	<.05	.41	.17	.98	.94	1.06
Constant	1.62	1.09	2.22	.14	5.06				

Table 10. Correlation Matrix for Continuous^1 and Discrete^0 Variables in the Treatment of Abnormal Behavior

	Sex^0	**Age^1**	**Rearing^0**	**Housing^1**	**Puzzle^0**	**Panel^0**	**Forage^0**	**Destrictuble^0**	**Nonfood^0**
Sex^0	-	-0.02	0.31	0.28	0.00	-0.32	0.09	-0.16	0.16
Age^1	-0.02	-	-0.14	0.31	-0.19	0.04	0.33	0.06	-0.20
Rearing^0	0.31	-0.14	-	0.06	-0.18	-0.12	-0.29	-0.34	0.20
Housing^1	0.28	0.31	0.06	-	-0.15	0.13	0.22	-0.19	-0.05
Puzzle^0	0.00	-0.19	-0.18	-0.15	-	-0.25	-0.18	0.03	-0.10
Panel^0	-0.32	0.04	-0.12	0.13	-0.25	-	0.22	-0.12	-0.09
Forage^0	0.09	0.33	-0.29	0.22	-0.18	0.22	-	0.21	-0.24
Destrictuble^0	-0.16	0.06	-0.34	-0.19	0.03	-0.12	0.21	-	-0.05
Nonfood^0	0.16	-0.20	0.20	-0.05	-0.10	-0.09	-0.24	-0.05	-

0 x 0 = polychoric / tetrachoric correlation
0 x 1 = polyserial correlation
1 x 1 = Pearson correlation

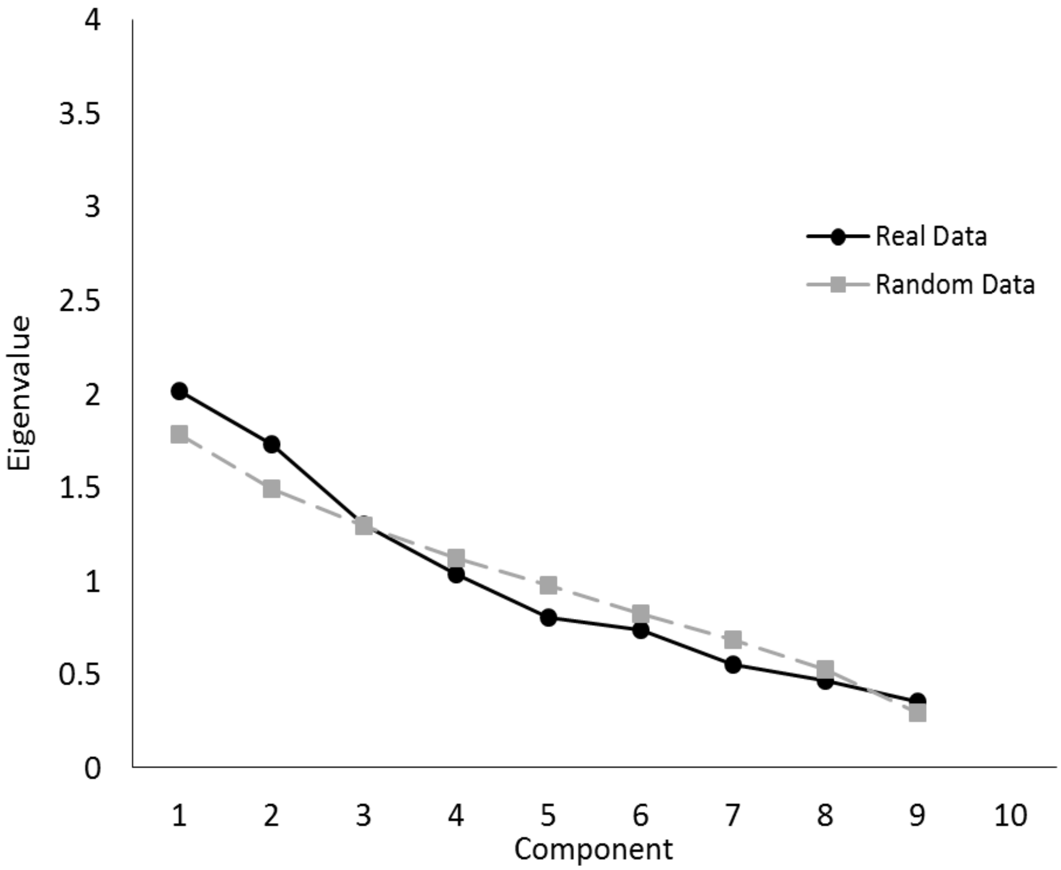

Figure 3. Scree plot showing the eigenvalues for each principal component extracted from the correlation matrix for the treatment of abnormal behavior data set ("Real Data," Table 10) and the mean eigenvalues of the bootstrapped parallel analysis ("Random Data").

Table 11. Principal Component Analysis Factor Loadings and Proportion of Variance Explained for Variables in the Treatment of Abnormal Behavior Data Set. Factor Loadings with Absolute Values > .5 are Bolded.

	Factor 1		**Factor 2**	
Variable	Factor Loadings	Variance Explained	Factor Loadings	Variance Explained
Sex	-0.35	0.12	**0.57**	0.32
Age	**0.57**	0.33	0.37	0.14
Rearing	**-0.62**	0.38	0.47	0.23
Single Housing	0.24	0.06	**0.71**	0.51
Puzzle	-0.21	0.04	-0.48	0.24
Visual barrier	0.44	0.20	0.12	0.01
Forage	**0.71**	0.51	0.25	0.06
Destructible	0.36	0.13	-0.47	0.22
Non-food	**-0.51**	0.26	0.10	0.01

Stereotypic Locomotor Behavior

Overall, there was no significant difference in percentage of observations in which stereotypic locomotor behavior was observed between the baseline (*M* = 20.8%, *SD* = 18.0%) and treatment (*M* = 22.2%, *SD* = 21.3%) periods, *t* (74) = -.74, *p* = .46. However, 52% of subjects did improve with treatment (as measured by a reduction in the percentage of scans in which stereotypic locomotor behavior was observed) while 48% did not improve (percentage of scans in which stereotypic locomotor behavior was observed increased or stayed the same).

Within this sample, prescribed treatments included additional forage (60% of subjects), non-food enrichment (46.7%), a visual barrier (36%), destructible enrichment items (32%), and a puzzle feeder (22%). Subjects averaged 2.4 treatments (*SD* = 1.0, range = 1 - 5), and the number of treatments did not vary between animals who improved and those who did not, *t* (73) = .22, *p* = .83.

Animals who displayed decreases in their stereotypic behavior had no significant difference in age (*t* (73) = -1.25, *p* = .22) or percentage of lifetime spent in single housing (*t* (73) = .09, *p* = .93) as compared with animals who did not improve. Neither sex (χ^2 (*df* = 1) = .90, *p* = .34) nor rearing (χ^2 (*df* = 2) = 1.22, *p* = .54) predicted whether or not animals would improve with treatment. When examined individually, no treatment variables predicted whether or not an animal's stereotypic locomotor behavior would improve (see Table 8).

A main-effects logistic regression model examining the relationship between all control and treatment predictor variables on the improvement of stereotypic locomotor behavior was not significant (χ^2 (*df* = 9) = 6.45, *p* = .69). No individual variables were significant predictors of improvement in stereotypic locomotor behavior (see Table 12). All tolerance levels were above .4, all VIFs were below 2.5 (Table 12), and all individual bivariate correlations were below .8 (see Table 13). Eigenvalues from the principal component analysis of the mixed correlation matrix were compared to the mean eigenvalues from a bootstrapped parallel analysis. This comparison resulted in the retention of two components (see Figure 4). The factor pattern was very similar to that seen with the abnormal behavior data set, with age at time of treatment, rearing history, additional forage enrichment, and non-food enrichment all loading moderate/high (absolute value > .5) on the first component. The second component included moderate/high loadings for sex and percentage of time spent in single housing. See Table 14 for factor loadings.

Table 12. Treatment of Stereotypic Locomotor Behavior: Logistic Regression Summary, Tolerance ("Tol."), and Variance Inflation Factor ("VIF").

Variable	B	SE	Wald	sig.	Exp(B)	95% CI		Tol.	VIF
Sex	-.49	.69	.50	.48	.62	.16	2.36	.75	1.34
Age	<.01	<.01	.95	.33	1.00	1.00	1.00	.75	1.33
Rearing	-.06	.36	.02	.88	.95	.47	1.92	.76	1.31
Single Housing	<-.00	.01	.13	.72	1.00	.97	1.02	.70	1.42
Puzzle	.34	.55	.40	.53	1.41	.49	4.10	.95	1.06
Visual barrier	-.67	.51	1.77	.18	.51	.19	1.38	.93	1.08
Forage	.21	.66	.10	.75	1.23	.34	4.49	.85	1.18
Destructible	.21	.55	.15	.70	1.23	.42	3.59	.89	1.12
Non-food	-.57	.52	1.21	.27	.57	.21	1.56	.88	1.13
Constant	.54	1.23	.19	.66	1.72				

Table 13. Correlation Matrix for Continuous^1 and Discrete^0 Variables in the Treatment of Stereotypic Locomotor Behavior

	Sex^0	**Age^1**	**Rearing^0**	**Housing^1**	**Puzzle^0**	**Panel^0**	**Forage^0**	**Destrictuble^0**	**Nonfood^0**
Sex^0	-	-0.09	0.45	0.34	0.04	-0.31	0.21	-0.15	0.29
Age^1	-0.09	-	-0.39	0.39	-0.11	0.02	0.42	0.14	-0.18
Rearing^0	0.45	-0.39	-	-0.10	-0.19	-0.16	-0.22	-0.37	0.29
Housing^1	0.34	0.39	-0.10	-	-0.14	0.07	0.34	-0.07	-0.17
Puzzle^0	0.04	-0.11	-0.19	-0.14	-	-0.15	0.06	0.00	-0.03
Panel^0	-0.31	0.02	-0.16	0.07	-0.15	-	0.14	-0.05	-0.23
Forage^0	0.21	0.42	-0.22	0.34	0.06	0.14	-	0.41	-0.35
Destrictuble^0	-0.15	0.14	-0.37	-0.07	0.00	-0.05	0.41	-	-0.02
Nonfood^0	0.29	-0.18	0.29	-0.17	-0.03	-0.23	-0.35	-0.02	-

0 x 0 = tetrachoric / polychoric correlation
0 x 1 = polyserial correlation
1 x 1 = Pearson correlation

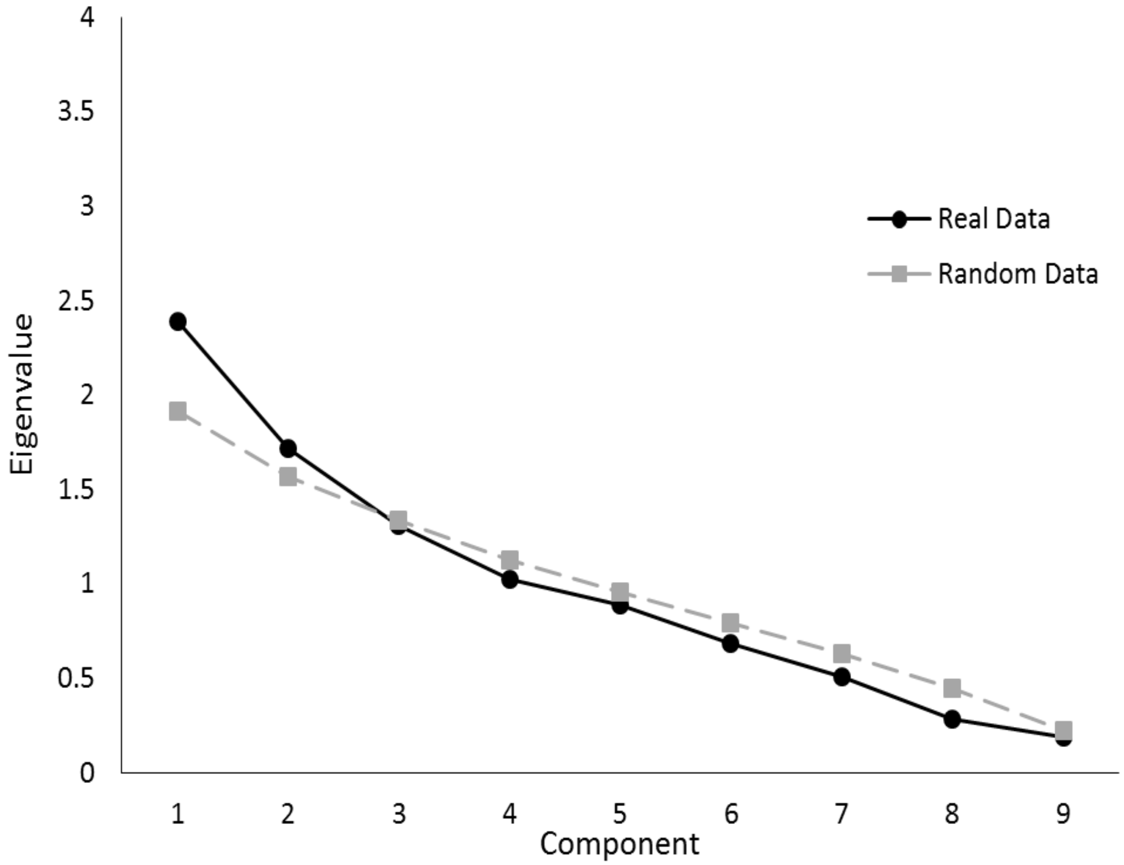

Figure 4. Scree plot showing the eigenvalues for each principal component extracted from the correlation matrix for the treatment of stereotypic locomotor behavior data set ("Real Data," Table 13) and the mean eigenvalues of the bootstrapped parallel analysis ("Random Data").

Table 14. Principal Component Analysis Factor Loadings and Proportion of Variance Explained for Variables in the Treatment of Stereotypic Locomotor Behavior Data Set. Factor Loadings with Absolute Values > .5 are Bolded.

	Factor 1		**Factor 2**	
Variable	Factor Loading	Variance Explained	Factor Loading	Variance Explained
Sex	-0.33	0.11	**0.84**	0.71
Age	**0.67**	0.45	0.29	0.08
Rearing	**-0.72**	0.52	0.36	0.13
Single Housing	0.39	0.15	**0.69**	0.48
Puzzle	<-0.01	<0.01	-0.13	0.02
Visual barrier	0.34	0.12	-0.28	0.08
Forage	**0.69**	0.47	0.43	0.08
Destructible	0.47	0.22	-0.12	0.01
Non-food	**-0.59**	0.35	0.13	0.02

Self-Biting

Overall, treatment did not reduce the percentage of scans in which self-biting was observed from baseline (*M* = 8.3%, *SD* = 14.5%) to treatment (*M* = 4.5%, *SD* = 6.8%, *t* (44) = 1.68, *p* = .101). Within self-biting subjects, 68.9% displayed improvement, while 31.1% displayed an increase or no change in the percentage of observations in which self-biting was observed.

Additional foraging opportunities were included in the treatment of 84.4% of subjects in the self-biting analysis. Visual barriers were provided to 51.1% of subjects, destructible enrichment was provided to 33.3% of subjects, non-food enrichment was provided to 31.1% of subjects, and puzzle feeders were prescribed to 24.4% of subjects.

There was no difference in age (*t* (43) = -.39, *p* = .70) or percentage of lifetime spent in single housing (*t* (43) = -.12, *p* = .91) between animals who did and did not improve. In addition, neither sex (χ^2 (*df* =1) = .47, *p* = .49) nor rearing history (χ^2 (*df* =2) = 1.23, *p* = .54) predicted improvement. When examined individually, no treatment component predicted improvement status (see Table 8).

A logistic regression model including control and predictor variables was not a significant fit for predicting self-biting improvement (χ^2 (*df* =8) = 4.64, *p* = .80). Additionally, no individual variable was predictive of improvement (see Table 15). All tolerance values were above .4 and all VIFs were below 2.5 (Table 15). Examination of the correlation matrix between predictors revealed no significant signs of multicollinearity (i.e., correlations above .8, see Table 16), and based on bootstrapped parallel analysis criteria, no dominant dimensions emerged following principal component analysis (see Figure 5).

Table 15. Treatment of Self-Biting Behavior: Logistic Regression Summary, Tolerance (“Tol.”), and Variance Inflation Factor (“VIF”).

Variable	**B**	**SE**	**Wald**	**sig.**	**Exp(B)**	**95% CI**		**Tol.**	**VIF**
Sex	-.14	.91	.02	.88	.87	.15	5.15	.77	1.30
Age	<.01	<.01	<.01	1.00	1.00	1.00	1.00	.84	1.19
Rearing	.39	.55	.51	.48	1.48	.51	4.3	.91	1.09
Single Housing	-.01	.02	.10	.75	1.00	.96	1.03	.84	1.20
Puzzle	-.37	.80	.21	.65	.69	.14	3.34	.97	1.03
Visual barrier	.06	.77	.01	.94	1.06	.24	4.74	.81	1.23
Forage	.12	1.01	.01	.91	1.12	.16	8.05	.93	1.08
Destructible	-.54	.73	.55	.46	.58	.14	2.44	.95	1.05
Non-food	-1.37	.79	3.00	.08	.25	.05	1.20	.83	1.21
Constant	1.21	1.92	.40	.53	3.37				

Table 16. Correlation Matrix for Continuous^1 and Discrete^0 Variables in the Treatment of Self-Biting

	Sex^0	**Age^1**	**Rearing^0**	**Housing^1**	**Puzzle^0**	**Panel^0**	**Forage^0**	**Destrictuble^0**	**Nonfood^0**
Sex^0	-	0.14	-0.06	0.09	0.13	-0.57	0.19	-0.07	0.37
Age^1	0.14	-	-0.01	0.29	-0.10	0.07	0.26	-0.15	-0.36
Rearing^0	-0.06	-0.01	-	-0.02	-0.04	-0.12	-0.32	-0.20	0.19
Housing^1	0.09	0.29	-0.02	-	-0.15	0.23	0.13	-0.17	-0.23
Puzzle^0	0.13	-0.10	-0.04	-0.15	-	-0.11	-0.08	0.06	-0.09
Panel^0	-0.57	0.07	-0.12	0.23	-0.11	-	0.13	-0.10	-0.02
Forage^0	0.19	0.26	-0.32	0.13	-0.08	0.13	-	0.09	0.05
Destrictuble^0	-0.07	-0.15	-0.20	-0.17	0.06	-0.10	0.09	-	0.06
Nonfood^0	0.37	-0.36	0.19	-0.23	-0.09	-0.02	0.05	0.06	-

0 x 0 = tetrachoric / polychoric correlation
0 x 1 = polyserial correlation
1 x 1 = Pearson correlation

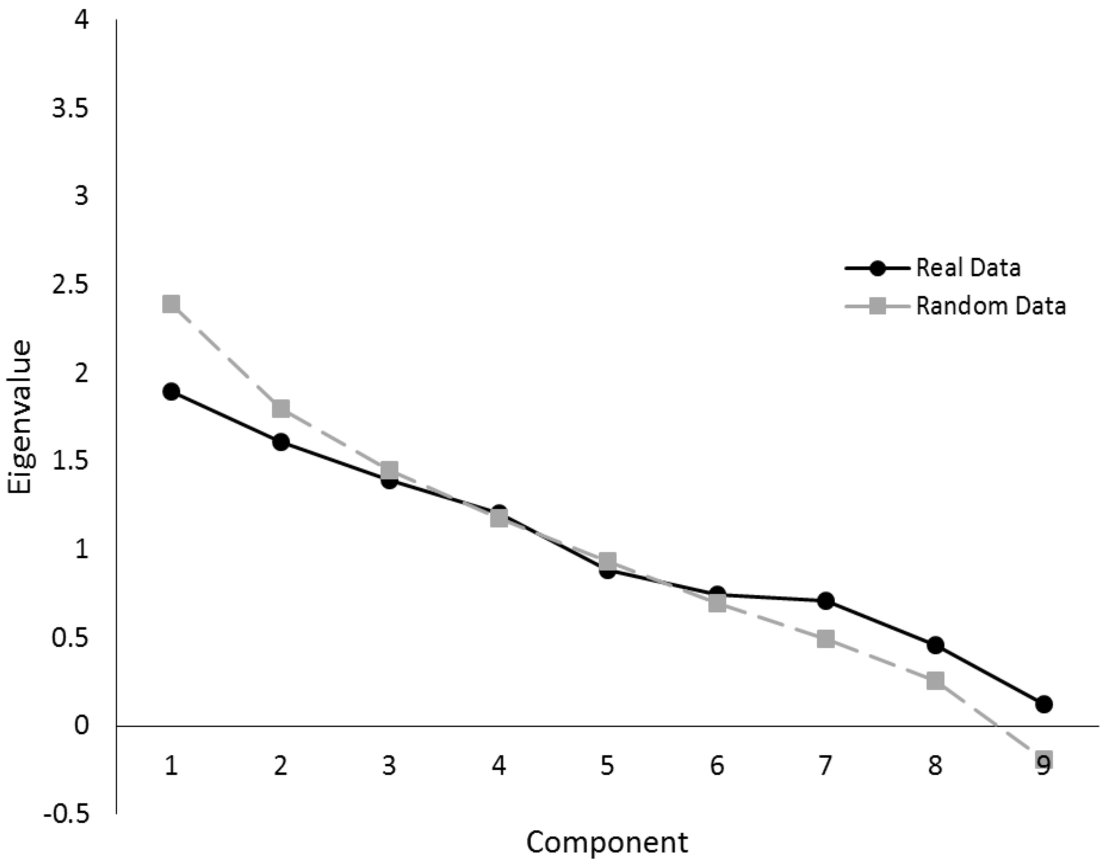

Figure 5. Scree plot showing the eigenvalues for each principal component extracted from the correlation matrix for the treatment of self-biting data set ("Real Data," Table 16) and the mean eigenvalues of the bootstrapped parallel analysis ("Random Data").

Discussion

I was unable to identify any animal traits (e.g., age, sex, rearing history, time spent in single housing) or treatment types that were consistently predictive of response to treatment. When looking at the overall improvement of abnormal behavior, there was some evidence that those animals receiving a non-food enrichment device (e.g., toys, mirrors, wood blocks) were less likely to improve than animals who did not receive these treatments. However, this effect did not hold up when stereotypic locomotor behavior and self-biting behaviors were examined individually.

It seems unlikely that non-food enrichment devices would actually hinder improvement. Instead, it may mean that, overall, non-food enrichment is less effective than the other treatment types tested in this model. Previous studies have shown that animals habituate quickly to non-food enrichment items (Line et al., 1991), and this could explain why these items could be less effective than other treatment types such as those involving food. Additionally, treatments were not distributed randomly to the subjects in these analyses. As evidenced by the principal component analysis results, some inter-dependency existed between the demographic and treatment variables. Thus, it is possible that animals given non-food enrichment devices may have differed from those not given non-food items on some unknown but important variables that affected their likelihood of improvement. Replication of these findings using prospective studies involving a higher level of experimental control is needed for confirmation of these results.

Several methodological issues limit the conclusions that can be drawn from these results. First, there was no control group to which we can compare the subjects going through treatment. This analysis could only look within those receiving treatment to see whether or not the type of treatment influenced the likelihood of improvement. It is not known whether animals not receiving behavioral treatments would have fared similarly or worse.

Second, the nature of the study (retrospective analysis of clinical data versus a prospective experiment) meant that treatments were not applied randomly amongst subjects and that various and unequal combinations of treatments were applied. In addition, as part of the YNPRC standard enrichment protocol, subjects in the baseline period would have had rotating access to many of the treatment types that were then later prescribed during the treatment period. Although prescribed treatments were above and beyond standard colony enrichment levels, previous exposure to devices may have limited their effect. A more thorough assessment of the effect of an individual treatment type on a topography of abnormal behavior would require a controlled experiment that could control for these factors.

Lastly, only the subjects' initial treatment plans were assessed. Within the YNPRC behavioral management program, subjects are frequently reassessed, and those subjects who do not respond to the initial treatment are prescribed different treatments. These reassessments and changes in treatments are done to maximize the clinical benefit to the animal. However, due to varying treatment and reassessment timelines, lack of stable baseline data, and small subject numbers, I was unable to analyze the effectiveness of these subsequent treatment interventions. Often, the first treatment interventions involve less-invasive and less labor-intensive interventions such as the addition of environmental enrichment. Subsequent treatment interventions are often more labor-intensive and involve treatments such as changes in housing, socializations, training, or behavioral medications. As the YNPRC behavioral monitoring program continues, we may reach a large enough sample size to permit analysis of these treatments in our population.

Overall, these findings are consistent with past research showing mixed results for enrichment and other treatment strategies for reducing abnormal behaviors (see Coleman et al., 2012 and Novak et al., 2012 for review) and also support the theory that, once abnormal behaviors develop, they can be resistant to treatment.

CHAPTER 6

ANALYSIS 4: TREATMENT EFFECTIVENESS IN REDUCING ALOPECIA

The aim of this archival analysis was to determine whether different types of treatment interventions improved the hair coat of rhesus macaques presenting with alopecia. The treatments analyzed in this analysis were identical to those in Analysis 3: additional foraging opportunities, puzzle feeders, non-food enrichment items, destructible enrichment items, and a visual barrier or privacy panel. This analysis included the control variables of sex (male/female), age (days at start of treatment), and current housing status (singly or pair housed).

Method

Subjects

The subject pool for this analysis was all rhesus macaques at YNPRC presenting with recent development or worsening of alopecia. To be included in the analysis, animals had to have received a behavioral treatment intervention due to receiving a hair score less than 4 (corresponding to 25% or more hair loss) and had to have received a re-evaluation of their hair coat following a stable period of treatment (i.e., with no treatment changes between hair scores).

Overall, 80 subjects (24 male / 56 female) met the criteria for inclusion in this analysis. All subjects were mother-reared. At the time treatment was initiated, 53.5% were in single housing and 47.5% were pair housed. A higher proportion of males (70.8%) than females (44.6%) were singly housed, χ^2 (*df* =1) = 4.62, *p* = .032. The average age of subjects was 3588 days / 9.8 years (*SD* = 2033 days, range = 735 – 9305 days or approximately 2 – 25 years). The variances of ages between males and females was unequal (Levene's test, $F = 11.42$, $p = .001$); therefore a corrected independent samples t-test was used to determine that females in this sample were significantly older ($M = 4161$days / 11.4 years, $SD = 2040$ days) than male subjects ($M = 2250$ days / 6.2 years, $SD = 1255$ days, t (68.1) = -4.249, p= < .001). On average, subjects in this sample had spent 17.3% of their lifetime in single housing at the time treatment was initiated ($SD = 22.4\%$, range = 0 – 93.9%). There was no difference in percentage of lifetime spent in single housing between males and females, t (78) = .338, $p = .736$.

Data Analysis

Animals were scored as to whether or not the prescribed treatment plan included each of five treatment types: additional foraging opportunities (e.g., seed, cereal or other forage provided on a forage board once or twice daily), the provision of feeding enrichment devices requiring the monkey to manipulate the device to remove food items (e.g., "puzzle feeders" such as challenger balls or peanut feeders), the addition of non-food enrichment items (e.g., toys that hang on the outside of the cage, mirrors, and wood blocks), destructible enrichment (e.g., paper or cardboard distributed once or twice daily), and the addition of a visual barrier or privacy panel. Most treatments consisted of multiple treatment types, so the pattern and number of treatments varied across subjects.

Hair scores conducted prior to the start of treatment and again following a period of stable treatment served as the data for this analysis. As described previously, hair scores range from 1 – 4, with a 4 reflecting a relatively full hair coat with less than 25% hair loss. Due to changes in hair score data collection protocols through the years, the time period between the initial low hair score and the re-evaluation of the hair coat ranged from 1 – 6 months post-treatment implementation (*M* = 107.1 days, *SD* = 48.2 days). Based on these hair scores, animals were scored as "improved" if the hair score increased from the baseline to treatment period or "not improved" if the hair scorestayed the same or decreased in treatment. The following variables were analyzed as control variables: sex (male/female), age (days at start of treatment), and current housing (single or pair).

The relationship between improvement in hair score and each control and treatment variable was first examined individually using either Pearson chi-square tests for categorical variables or independent-samples t-tests for continuous variables. The significance level was set at .05 for all tests. Then, treatment and control variables were entered into a main-effects logistic regression model in which the outcome variable was improvement/no improvement. As in previous analyses, multicollinearity was assessed by examination of the correlation matrix and the calculation of tolerance and VIF for each variable. The correlation matrix consisted of a mixture of polyserial correlations (binary*continuous variables) and tetrachoric correlations (binary*binary variables). Principal component analyses were then calculated from the resulting correlation matrix, and a bootstrapped version of Horn's (1965) parallel analysis criteria (Buja & Eyuboglu, 1992) was used to determine retention of components.

Results

Overall, 61.3% of subjects saw improvement in their hair score with treatment. The average hair score increased significantly between baseline (*M* = 2.69, *SD* = .54) and treatment (*M* = 3.23, *SD* = .84, paired-samples t-test, t (79) = -6.05, $p < .001$). Additional forage was prescribed for the majority (87.5%) of subjects. In addition, 31.3% of subjects received puzzle feeders, 27.5% received non-food enrichment devices, 20% received destructible enrichment items, and 13.8% received a visual barrier. The average number of treatments per subject was 1.8 (*SD* = 0.8, range 1 – 5). The number of treatment types did not differ significantly between animals who improved (*M* = 1.84 *SD* = .90) and those who did not (*M* = 1.74, *SD* = .6, paired-samples t-test, *t* (79) = -.513, *p* = .610).

Neither sex (χ^2 (*df* =1) = 1.327, *p* = .249) nor current housing status (χ^2 (*df* =1) = .343, *p* = .558) was related to improvement in alopecia. The variance in ages of animals were unequal between improvement categories (Levene's test, *F* = 5.7, *p* = .019), but a correct independent-samples t-test revealed no significant difference in age between animals who improved with treatment and those who did not, *t* (52.2) = 1.45, *p* = .128. When examined individually, only non-food enrichment showed a significant relationship with improvement status (χ^2 (*df* =1) = 5.41, *p* = .02. Animals receiving non-food enrichment were more likely to improve (odds ratio = 3.9) than those who did not (see Table 17).

Table 17. Summary of Pearson Chi-Square Tests and Odds Ratios for Treatment Type (Additional Forage, Puzzle Feeders, Non-Food Enrichment, Destructible Enrichment, and Visual Barrier) and Improvement of Alopecia

		Forage	**Puzzle**	**Non-Food**	**Destruct.**	**Visual barrier**
Alopecia	Chi-Square	0.01	0.42	5.41	0.21	0.24
	sig	0.93	0.52	0.02	0.65	0.62
	Odds Ratio	1.06	0.73	3.92	0.77	0.72
	95% CI	0.27	0.28	1.18	0.25	0.20
		4.11	1.90	13.01	2.34	2.62

The main-effects logistic regression model containing control variables (age, sex, current housing) and predictor variables (treatment type) was not significant, χ^2 (*df* = 8) = 9.17, *p* = .328. Within the model, only non-food enrichment was a significant predictor of improvement, with animals receiving non-food enrichment being significantly more likely to improve (odds ratio/exp(B) = 4.06, Wald $\chi 2$ (*df* = 1) = 4.8, *p* = .029). No other predictor reached statistical significance (see Table 18). No significant multicollinearity was detected in the model: all tolerance values were above .4, all VIFs were below 2.5 (see Table 18), and no bivariate correlations between predictor variables exceeded .8 (Table 19). Based on bootstrapped parallel analysis criteria, no dominant dimensions emerged following principal component analysis (see Figure 6).

Table 18. Treatment of Alopecia: Logistic Regression Summary, Tolerance (“Tol.”), and Variance Inflation Factor (“VIF”).

Variable	B	SE	Wald	sig.	Exp(B)	95% CI		Tol.	VIF
Sex	-.25	.67	.14	.70	.78	.21	2.88	.65	1.54
Age	<.01	<.01	1.13	.29	1.00	1.00	1.00	.63	1.59
Housing	-.42	.56	.56	.46	.66	.22	1.99	.76	1.32
Puzzle	-.15	.53	.08	.78	.86	.31	2.43	.93	1.08
Visual barrier	-.04	.73	<.01	.95	.96	.23	3.99	.91	1.10
Forage	-.24	.79	.09	.76	.79	.17	3.70	.84	1.19
Destructible	-.06	.68	<.01	.94	.95	.25	3.60	.79	1.27
Non-food	1.40	.64	4.80	.03	4.06	1.16	14.21	.95	1.06
Constant	2.04	1.34	2.32	.13	7.68				

Table 19. Correlation Matrix for Continuous^{1} and Discrete^{0} Variables in the Treatment of Alopecia

	Sex^{0}	**Age^{1}**	**Housing^{1}**	**Puzzle^{0}**	**Panel^{0}**	**Forage^{0}**	**Destructible^{0}**	**Nonfood^{0}**
Sex^{0}	-	0.64	0.39	-0.05	0.23	0.32	-0.03	0.07
Age^{1}	0.64	-	-0.21	0.02	0.31	0.05	0.31	-0.08
Housing^{1}	0.39	-0.21	-	0.01	-0.32	-0.19	0.27	0.05
Puzzle^{0}	-0.05	0.02	0.01	-	0.24	-0.30	-0.13	-0.32
Panel^{0}	0.23	0.31	-0.32	0.24	-	-0.16	0.15	-0.19
Forage^{0}	0.32	0.05	-0.19	-0.30	-0.16	-	-0.51	0.37
Destrictuble^{0}	-0.03	0.31	0.27	-0.13	0.15	-0.51	-	-0.05
Nonfood^{0}	0.07	-0.08	0.05	-0.32	-0.19	0.37	-0.05	-

0 x 0 = tetrachoric correlation
0 x 1 = polyserial correlation

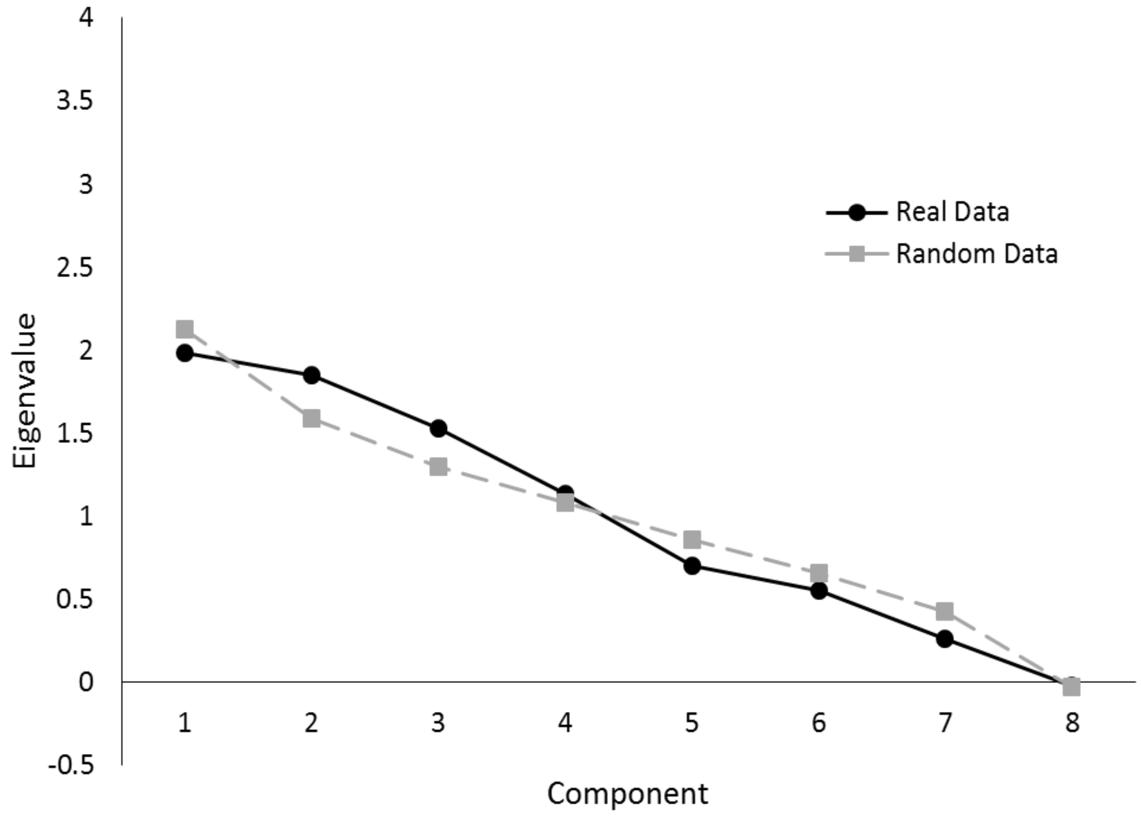

Figure 6. Scree plot showing the eigenvalues for each principal component extracted from the correlation matrix for the treatment of alopecia data set ("Real Data," Table 19) and the mean eigenvalues of the bootstrapped parallel analysis ("Random Data").

Discussion

As in the previous analysis, the conclusions that can be drawn from these results are limited by the nature of the data. The analysis of archival treatment data meant that there were inconsistencies in the number of subjects prescribed various treatments and also in the interval between reassessment of alopecia. For example, the large majority (87.5%) of subjects received additional forage as a treatment. This limits the ability to determine whether not receiving forage would have led to worse outcomes. The inconsistent time periods between assessment and reassessment of the hair coat could also influence outcomes. Ideally, the effectiveness of these treatments on alopecia would be studied using a carefully planned, prospective experiment in which there is a control group not receiving treatment and in which treatments are randomly assigned across factors such as sex, age, and severity of alopecia.

The addition of a control group would also rule out improvement of hair coat based on factors unrelated to behavioral treatment, such as seasonal variation. Previous studies have found a relationship between season and hair coat in NHP (Beisner & Isbell, 2009; Lutz & Sharp, 2015; Steinmetz et al., 2006). While the season in which treatment was administered was not factored into this analysis, subsequent examination of the data revealed that the low hair scores that initiated treatment were split relatively equally between fall/winter (52.5%) and spring/summer (47.5%) in this sample. The season in which treatment was initiated (fall/winter or spring/summer) was not related to alopecia improvement (Pearson chi-square, χ^2 (df =1) = .628, p = .428). In addition, an analysis of quarterly (January, April, July, and October) hair scores collected on 311 cage-housed rhesus macaques at YNPRC from 2013 through 2014 showed no difference in hair scores across the seasons (Friedman's test, *p* = .147). Therefore, I believe that seasonal variation was unlikely to have a large influence in this population.

This analysis did allow an examination of current practices in the treatment of alopecia at YNPRC to determine whether any treatment types were predictive of improvement in hair coats. Overall, the model investigating the effect of different treatment types on improvement of alopecia was not significant. Rather surprisingly, the addition of non-food enrichment, a category that included mirrors, triangles, and wood blocks hung on the outside of cages, did appear to increase the chances that a subject's hair coat would improve with treatment. In a previous study examining the behavior of rhesus macaques given access to a highly-enriched play cage, we found that the mirror was the most-used enrichment device, out-performing devices such as forage boards and puzzle feeders (Griffis et al., 2013). If animals spend a significant portion of their time manipulating non-food enrichment devices such as mirrors, this could offer a competing behavior to hair plucking and/or reduce stress levels that may be associated with alopecia.

However, previous studies have shown rapid habituation to mirrors (Clarke, Czekala, & Lindburg, 1995; Gallup & Suarez, 1991) and other non-food enrichment items such as rubber dog toys and wooden sticks (Line et al., 1991). That, combined with previous findings that non-food enrichment items showed no reduction in abnormal behavior (Line et al., 1991) and the findings in Analysis 2 that showed that non-food items were actually predictive of worse improvement outcomes for abnormal behaviors, suggests that caution is advised when interpreting these results. This result could be a spurious finding resulting from the lack of experimental control allowed by the retrospective nature of this analysis. For example, perhaps non-food enrichment devices were given to animals showing less severe alopecia and, thus, these animals were more likely to display an improved hair coat on follow up. However, given the findings suggesting a relationship between non-food enrichment items and improvement in hair coat, a more carefully-controlled, prospective study involving random assignment of non-food enrichment devices across a treatment and control group may be warranted in order to better test the effects of these enrichment devices on alopecia.

CHAPTER 7: SUMMARY AND CONCLUDING DISCUSSION

The examination of behavioral predictors of self-wounding revealed that the display of self-biting, hair plucking, and, to some degree, floating limb and self-oral behaviors, was predictive of future self-wounding. Importantly, these behaviors occurred during the year preceding the animal's first incident of self-wounding. Thus, the presence of these behaviors identifies animals as being at risk of future self-wounding and may give behavioral managers the opportunity to intervene before wounding occurs.

For alopecia, fear behaviors may be predictive of the future development of hair loss. No other behaviors were found to predict the subsequent development of alopecia. However, an inverse relationship was found between the display of stereotypic locomotor behaviors and the development of alopecia, with animals displaying behaviors such as ritualized pacing and flipping being less likely to go on to develop significant hair loss. These findings contribute to the understanding of self-wounding and alopecia in captive NHP. The results will help guide refinements in the behavioral monitoring program at YNPRC such that more animals can be identified for behavioral evaluation and treatment before self-wounding or significant hair loss occurs.

It would seem that the identification of at-risk animals may be an easier task than the treatment of their behavioral disorders. The results of my analyses did not identify animal characteristics (e.g., age, sex) or specific types of treatment that reliably predict whether or not an animal's abnormal behavior or alopecia would improve. With one exception (the addition of non-food enrichment increasing the chances of improvement for animals with alopecia), the results do not allow me to make a specific recommendation to a behavioral manager about what type of environmental enrichment might be best for an animal displaying a particular behavioral issue.

For the treatment analyses, the outcome variable was dichotomous (i.e., improved or did not improve). In some cases, a small decrease in the frequency or duration of an abnormal behavior may not be clinically significant. For example, in the analysis examining the effects of treatment on stereotypic locomotor behavior, an animal that went from pacing in 80% of observations to pacing in 75% of observations would be considered “improved.” However, that level of improvement may not reflect any meaningful increase in that animal’s psychological wellbeing. Defining what degree of improvement is meaningful for any particular behavior or individual comes with many challenges. However, future analyses could examine improvement on a more continuous scale or defined in a manner that better allows for analysis of what factors lead to clinically significant improvement.

The most commonly applied treatments at YNPRC included the addition of visual barriers and various types of environmental enrichment (e.g., feeding enrichment including forage board and puzzle feeders, non-food items such as mirrors or wood blocks, and destructible items such as paper). These treatments have the benefit of being relatively easy to apply in the laboratory setting. However, given my results showing little difference in the improvement of abnormal behavior or alopecia between these treatment types, I would recommend that future efforts focus on implementing and assessing treatment plans that also include other treatments such as training and socialization.

Socialization and training are more labor-intensive and more difficult to implement due to personnel time, facility resources, and research requirements. However, previous studies have shown them to be beneficial. Moving animals to social housing has been found to be effective in reducing both SIB (Line et al., 1990; Reinhardt, 1999; Weed et al., 2003) and alopecia (Harding, 2013). Additionally, since fear was found to be associated with alopecia in the YNPRC population, there is reason to believe that desensitization training (e.g., Clay, Bloomsmith, Marr, & Maple, 2009) could be effective in preventing the development of alopecia in some animals. While general exposure to positive reinforcement training did not reduce SIB in rhesus macaques (Baker et al., 2009), future studies could incorporate a broader, behavior analytic framework in which operant conditioning techniques are used to specifically target the abnormal behaviors. For example, functional analysis techniques have been used to assess and subsequently reduce SIB, feces-throwing, and aggression in captive NHP (Dorey, Rosales-Ruiz, Smith, & Lovelace, 2009; Farmer-Dougan, 2014; Martin, Bloomsmith, Kelley, Marr, & Maple, 2011). Future studies could focus on identifying the underlying operant functions of abnormal behaviors in captive primates. If the underlying function (e.g., an increase or decrease in arousal or tension) could be identified, treatments that offer an alternative and more adaptive way of meeting the animal’s needs could be identified (see Martin, 2015).

Even though my analysis did not identify specific forms of environmental enrichment that reliably decreased abnormal behaviors or improve alopecia, this does not necessarily indicate that these treatments are ineffective or should be removed. As reviewed by Coleman et al. (2012), environmental enrichment may still prevent the development or worsening of these conditions and contribute to increased wellbeing through the opportunity to engage in more species-typical behaviors. The reduction of abnormal behavior is only one element in psychological wellbeing. The environmental enrichment provided at YNPRC is likely to have other benefits such as increasing species-typical behavior and reducing overall stress.

The data set for this study did result in some limitations for these conclusions. The behavioral observations that served as the basis for these analyses may not have captured times when abnormal behaviors temporarily decreased after the addition of an enrichment device or foraging opportunity (e.g., Gottlieb et al., 2011; Novak et al., 1998). Instead, this analysis only provided information about the subjects' overall patterns of behavior. Additionally, the behavioral data are somewhat of a convenience sample, with observation periods differing on important variables such as time of day and length of observation period. While this is less than ideal for rigorous scientific control, it does offer great practical use. The BMU personnel observing the animals as part of their daily walk-throughs are viewing the animals in much the same way that animal care staff and veterinarians view animals in a laboratory setting on any particular day. Therefore, the ability to identify and monitor key behaviors in this manner is especially practical.

The display of abnormal behaviors and alopecia in captive primates raises serious concerns about the psychological wellbeing of this population. In addition, the assessment and treatment of these behaviors in captive primates involves significant personnel and financial costs. The information gained from this study may allow for better identification of at-risk animals in order to improve both the effectiveness and efficiency of the monitoring and treatment of abnormal behaviors and alopecia in captive primates.

APPENDIX

ABNORMAL BEHAVIOR ETHOGRAM

Behavioral Category	**Definition / Examples**
Bizarre posture (BIZ)	Holding seemingly uncomfortable or unnatural position. An example would be hind leg extensions
Self-oral behavior (ORAL)	Self-directed behavior involving oral contact with one's own body. This includes digit-sucking and mouthing.
Fecal behaviors (FEC)	Smearing or rubbing fecal material onto a surface; coprophagy (ingestion of fecal material)
Fear behaviors (FEAR)	Behaviors associated with escape or avoidance. Examples of fearful behaviors in nonhuman primates include fearful facial expressions, crouching, cringing, and freezing. Fear behaviors are associated with a specific triggering stimulus (e.g., a person walking in the room, a threat from another primate, etc.).
Floating limb (FLO)	Animal raises limb in the air and appears not to be in control of the limb. It is often accompanied by slow, repetitive brushing of the coat by the digits of the elevated limb. Animal may threaten and/or subsequently bite the limb.
Hair plucking (HPS)	Pulling out of one's own hair. Often repetitive, may or may not be followed by ingestion of the hair.
Other self-directed stereotyped behaviors (SSY)	Repetitive and ritualistic behaviors that are directed at an animal's own body and not otherwise specified in the ethogram. Examples include self-clasping, rocking, swaying, skin pulling, and head-tossing.
Other self-injurious behavior (OSIB)	Any self-injurious behavior not otherwise specified by this ethogram. Examples may include self-slapping or head-banging.
Regurgitate/re-ingest (R&R)	Animal vomits food or liquid and ingests vomited material
Self-biting (BTE)	Closing the teeth rapidly and with force on one's self. The bite may or may not break the skin.
Self-directed eye behaviors (EYE)	This category includes eye poking (digit in eye socket), saluting (raising hand to the eye on the same side with the fingers in a position that resembles a salute, possibly with the thumb pressing against the eyeball), and eye covering (covering eye(s) with one or both hands)
Stereotypic locomotor behaviors (SLO)	Repetitive behavior patterns involving movement that does not serve an obvious function such as those involved in playing, grooming, etc. These behaviors include, but are not limited to flipping, pacing, circling, and repetitive swinging.
Urophagy (URI)	Licking or sucking of urine either directly from the penis or pooled on a surface.

REFERENCES

Allison, P. D. (2012). *Logistic regression using SAS: Theory and application* (2nd ed.). Cary, N.C.: SAS Institute Inc.

Baker, K. C. (2004). Benefits of positive human interaction for socially housed chimpanzees. *Animal Welfare, 13,* 239-245.

Baker, K. C., Bloomsmith, M. A., Neu, K., Griffis, C., & Maloney, M. (2010). Positive reinforcement training as enrichment for singly housed rhesus macaques (*Macaca mulatta*). *Animal Welfare, 19,* 307-313.

Baker, K. C., Bloomsmith, M. A., Neu, K., Griffis, C., Maloney, M., Oettinger, B., . . . Martinez, M. (2009). Positive reinforcement training moderates only high levels of abnormal behavior in singly housed rhesus macaques. *Journal of Applied Animal Welfare Science, 12,* 236-252. doi: 10.1080/10888700902956011

Baker, K. C., Bloomsmith, M. A., Oettinger, B., Neu, K., Griffis, C., Schoof, V. A. M., & Maloney, M. (2012). Benefits of pair housing are consistent across a diverse population of rhesus macaques. *Applied Animal Behaviour Science, 137,* 148-156. doi: http://dx.doi.org/10.1016/j.applanim.2011.09.010

Baker, K. C., Weed, J. L., Crockett, C. M., & Bloomsmith, M. A. (2007). Survey of environmental enhancement programs for laboratory primates. *American Journal of Primatology, 69,* 377-394.

Bayne, K., Dexter, S., & Suomi, S. (1992). A preliminary survey of the incidence of abnormal behavior in rhesus monkeys (*Macaca mulatta*) relative to housing condition. *Lab Animal (USA), 21*(5), 38-46.

Bayne, K., Mainzer, H., Dexter, S., Campbell, G., Yamada, F., & Suomi, S. (1991). The reduction of abnormal behaviors in individually housed rhesus monkeys (*Macaca mulatta*) with a foraging/grooming board. *American Journal of Primatology, 23,* 23-35. doi: 10.1002/ajp.1350230104

Beisner, B. A., & Isbell, L. A. (2008). Ground substrate affects activity budgets and hair loss in outdoor captive groups of rhesus macaques (*Macaca mulatta*). *American Journal of Primatology, 70,* 1160-1168. doi: 10.1002/ajp.20615

Beisner, B. A., & Isbell, L. A. (2009). Factors influencing hair loss among female captive rhesus macaques (*Macaca mulatta*). *Applied Animal Behaviour Science, 119,* 91-100. doi: doi: http://dx.doi.org/10.1016/j.applanim.2009.03.016

Bentson, K. L., Crockett, C. M., Wahl, K. L., Runeson, E. P., Bellanca, R. U., Lee, G. H., . . . Ha, J. C. (2010). Floating limb behaviors and self-biting are associated in laboratory monkeys. *American Journal of Primatology, 72*, 725-733. doi: 10.1002/ajp.20831

Berkson, G. (1968). Development of abnormal setereotyped behaviors. *Developmental Psychobiology, 1,* 118-132.

Birkett, L. P., & Newton-Fisher, N. E. (2011). How abnormal is the behaviour of captive, zoo-living chimpanzees? *PloS One, 6*(6), e20101. doi: 10.1371/journal.pone.0020101

Bloomsmith, M. A., Alford, P. L., & Maple, T. L. (1988). Successful feeding enrichment for captive chimpanzees. *American Journal of Primatology, 16*, 155-164. doi: 10.1002/ajp.1350160206

Boccia, M. L., & Hijazi, A. S. (1998). A foraging task reduces agonistic and stereotypic behaviors in pigtail macaque social groups. *Laboratory Primate Newsletter, 37,* 1-4.

Buja, A. & Eyuboglu, N. (1992). Remarks on parallel analysis. *Multivariate Behavioral Research, 27,* 509-540.

Byrne, G. D. & Suomi, S. (1991). Effects of woodchips and buried food on behavior patterns and psychological well-being of captive rhesus monkeys. *American Journal of Primatology, 23*, 141 – 151.

Christenson, G. A., Mackenzie, T. B., & Mitchell, J. E. (1991). Characteristics of 60 adult chronic hair pullers. *The American Journal of Psychiatry, 143,* 365-370.

Clarke, A. S., Czekala, N. M., & Lindburg, D. G. (1995). Behavioral and adrenocortial responses of male cynomolgus and lion-tailed macaques to social stimulation and group formation. *Primates, 36,* 41 – 56.

Clarke, A. S., Juno, C. J., & Maple, T. L. (1982). Behavioral effects of a change in the physical environment: A pilot study of captive chimpanzees. *Zoo Biology, 1,* 371-380. doi: 10.1002/zoo.1430010411

Clay, A. W., Bloomsmith, M. A., Marr, M. J., & Maple, T. L. (2009). Habituation and desensitization methods for reducing fearful behavior in singly housed rhesus macaques. *American Journal of Primatology, 71,* 30 – 39. doi: 10.1002/ajp.20622

Coble, D. C., Martin, A. L., Perlman, J. E., Strait, K. R., Wilson, M. E., & Bloomsmith, M. A. (2010). Rate of self-injurious behavior in Buspirone-treated rhesus macaques (*Macaca mulatta*) across different levels of human activity in the environment. [Abstract]. *American Journal of Primatology, 72(S1)*, 27-28.

Coleman, K., Bloomsmith, M. A., Crockett, C. M., Weed, J. L., & Schapiro, S. J. (2012). Behavioral management, enrichment, and psychological well-being of laboratory nonhuman primates. In C. R. Abee, K. Mansfield, S. Tardif & T. Morris (Eds.), *Nonhuman primates in biomedical research: Biology and management (*2nd Ed, Vol. 1, pp. 149 - 176). Waltham, MA: Elsevier.

Coleman, K., Lutz, C. K., Worlein, J. M., Gottlieb, D. H., Peterson, E., Lee, G. H., . . . Novak, M. A. (2015). The correlation between alopecia and temperament in rhesus macaques (*Macaca mulatta*) at four primate facilities. *American Journal of Primatology.* Advance online publication. doi: 10.1002/ajp.22504

Coleman, K., & Maier, A. (2010). The use of positive reinforcement training to reduce stereotypic behavior in rhesus macaques. *Applied Animal Behaviour Science, 124,* 142-148.

Crast, J., Bloomsmith, M., Perlman, J., Meeker, T., & Remillard, C. (2014). Abnormal behaviour in captive sooty mangabeys. *Animal Welfare, 23*, 167-177.

Crockett, C. M., Bowers, C. L., Shimoji, M., Leu, M., Bowden, D. M., & Sackett, G. P. (1995). Behavioral responses of longtailed macaques to different cage sizes and common laboratory experiences. *Journal of Comparative Psychology, 109*, 368 - 383.

Davenport, M. D., Lutz, C. K., Tiefenbacher, S., Novak, M. A., & Meyer, J. S. (2008). A rhesus monkey model of self injury: effects of relocation stress and neuroendocrine function. *Biological Psychiatry, 63*, 990-996.

Dorey, N. R., Rosales-Ruiz, J., Smith, R., & Lovelace, B. (2009). Functional analysis and treatment of self-injury in a captive olive baboon. *Journal of Applied Behavior Analysis, 42*, 785-794.

Eaton, G. G., Kelley, S. T., Axthelm, M. K., Iliff-Sizemore, S. A., & Shiigi, S. M. (1994). Psychological wellbeing in paired adult female rhesus (*Macaca mulatta*). *American Journal of Primatology, 33*, 89-99.

Ekstrom, J. (2008). The phi-coefficient, the tetrachoric correlation coefficient, and the Pearson-Yule debate. Retrieved from http://statistics.ucla.edu/preprints/uclastat-preprint-2008:40

Erwin, J., & Deni, R. (1979). Strangers in a strange land: Abnormal behaviors or abnormal environments. In J. Erwin, T. L. Maple & G. Mitchell (Eds.), *Captivity and behavior: Primates in breeding colonies,laboratories, and zoos* (pp. 1 - 28). New York: Van Nostrand Reinhold Company.

Farmer-Dougan, V. (2014). Functional analysis of aggression in a black-and-white ruffed lemur (*Varecia variegata variegata*). *Journal of Appplied Animal Welfare Science, 17*, 282 – 293.

Fekete, J. M., Norcross, J. L., & Newman, J. D. (2000). Artificial turf foraging boards as environmental enrichment for pair-housed female squirrel monkeys. *Journal of the American Association for Laboratory Animal Science, 39*(2), 22-26.

Fontenot, M. B., Musso, M. W., McFatter, R. M., & Anderson, G. M. (2009). Dose-finding study of fluoxetine and venlafaxine for the treatment of self-injuious and stereotypic behavior in rhesus macaques (*Macaca mulatta*). *Journal of the American Associaton for Laboratory Animal Science, 48,* 176 – 184.

Fontenot, M. B., Padgett III, E. E., Dupuy, A. M., Lynch, C. R., De Petrillo, P. B., & Higley, J. D. (2005). The effects of fluoxetine and buspirone on self-injurious and stereotypic behavior in adult male rhesus macaques. *Comparative Medicine, 55,* 67-74.

Fontenot, M. B., Wilkes, M. N., & Lynch, C. S. (2006). Effects of outdoor housing on self-injurious and stereotypic behavior in adult male rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science, 45*(5), 35-43.

Gallup, G. G. Jr. & Suarez, S. D. (1991). Social responding to mirrors in rhesus monkeys (*Macaca mulatta*): effects of temporary mirror removal. *Journal of Comparative Psychology*, *105,* 376 – 379.

Garner, J. P. (2005). Stereotypies and other abnormal repetitive behaviors: Potential impact on validity, reliability, and replicability of scientific outcomes. *ILAR journal / National Research Council, Institute of Laboratory Animal Resources, 46,* 106 - 117.

Gottlieb, D. H., Capitanio, J. P., & McCowan, B. (2013). Risk factors for stereotypic behavior and self-biting in rhesus macaques (*Macaca mulatta*): Animal's history, current environment, and personality. *American Journal of Primatology, 75,* 995-1008.

Gottlieb, D. H., Ghirardo, S., Minier, D. E., Sharpe, N., Tatum, L., & McCowan, B. (2011). Efficacy of 3 types of foraging enrichment for rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science, 50,* 888 – 894.

Griffis, C. M., Martin, A. L., Perlman, J. E., & Bloomsmith, M. A. (2013). Play caging benefits the behavior of singly housed laboratory rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science, 52,* 534-540.

Hannibal, D., Cassidy, L., Day, A., Tatum, L., & McCowan, B. (2013). Increased produce enrichment reduces alopecia in captive outdoor socially-housed rhesus macaques (*Macaca mulatta*) [Abstract]. *American Journal of Primatology, 75 (S1),* 92.

Harding, K. (2013). Behavior treatment of alopecia in *Macaca fascicularis*: comparisons of outcomes. [Abstract]. *American Journal of Primatology, 75(S1),* 51.

Harlow, H. F., & Harlow, M. K. (1962). The effect of rearing conditions on behavior. *Bulletin of the Menninger Clinic*, *26*, 213-224.

Hopper, L. M., Freeman, H. D., Ross, S. R. (in press). Reconsidering coprophagy as an indicator of negative welfare for captive chimpanzees. *Applied Animal Behavior Science*. Advance Online Publication. doi: http://dx.doi.org/10.1016/j.applanim.2016.01.002

Horn, J. L. (1965). A rationale and test for the number of factors in factor analysis. *Psychometrica, 30,* 175-189.

Hsieh, F. Y., Bloch, D. A., & Larson, M. D. (1998). A simple method of sample size calculation for linear and logistic regression. *Statistics in Medicine, 17*, 1623-1634.

Huneke, R. B., Foltz, C. J., VandeWoude, S., Mandrell, T. D., & Garman, R. H. (1996). Characterization of dermatologic changes in geriatric rhesus macaques. *Journal of Medical Primatology, 25*, 404-413.

Ijichi, C. L., Collins, L. M., & Elwood, R. W. (2013). Evidence for the role of personality in stereotypy predisposition. *Animal Behaviour, 85,* 1145-1151.

Kaufman, B. M., Pouliot, A. L., Tiefenbacher, S., & Novak, M. A. (2004). Short and long-term effects of a substantial change in cage size on individually housed, adult male rhesus monkeys (*Macaca mulatta*). *Applied Animal Behaviour Science, 88*, 319-330. doi: http://dx.doi.org/10.1016/j.applanim.2004.03.012

Kempf, D. J., Baker, K. C., Gilbert, M. H., Blanchard, J. L., Dean, R. L., Deaver, D. R., & Bohm, R. P. (2012). Effects of extended-release injectable naltrexone on self-injurious behavior in rhesus macaques (*Macaca mulatta*). *Comparative Medicine, 62*, 209-217.

Kessel, A. L., & Brent, L. (1998). Cage toys reduce abnormal behavior in indvidually housed pigtail macaques. *Journal of Applied Animal Welfare Science, 1,* 227 – 235.

Kessel, A., & Brent, L. (2001). The rehabilitation of captive baboons. *Journal of Medical Primatology, 30,* 71 – 80.

Kleinbaum, D. G., & Klein, M. (2002). *Logistic regression: A self-learning text* (2nd ed.). New York: Springer-Verlag New York, Inc.

Kramer, J., Fahey, M., Santos, R., Carville, A., Wachtman, L., & Mansfield, K. (2010). Alopecia in rhesus macaques correlates with immunophenotypic alterations in dermal inflammatory infiltrates consistent with hypersensitivity etiology. *Journal of Medical Primatology, 39,* 112 – 122. doi:10.1111/j.1600-0684.2010.00402.x

Kramer, J. A., Mansfield, K. G., Simmons, J. H., & Bernstein, J. A. (2011). Psychogenic alopecia in rhesus macaques presenting as focally extensive alopecia of the distal limb. *Comparative Medicine, 61,* 263-268.

Kroeker, R., Bellanca, R. U., Lee, G. H., Thom, J. P., & Worlein, J. M. (2014). Alopecia in three macaque species housed in a laboratory environment. *American Journal of Primatology, 76,* 325-334.

Line, S. W., Morgan, K. N., & Markowitz, H. (1991). Simple toys do not alter the behavior of aged rhesus monkeys. *Zoo Biology, 10,* 473 – 484.

Line, S. W., Morgan, K. N., Markowitz, H., Roberts, J., & Riddell, M. (1990). Behavioral responses of female long-tailed macaques (*Macaca fascicularis*) to pair formation. *Laboratory Primate Newsletter, 29(4),* 1.

Luchins, K. R., Baker, K. C., Gilbert, M. H., Blanchard, J. L., Liu, D. X., Myers, L., & Bohm, R. P. (2011). Application of the diagnostic evaluation for alopecia in traditional veterinary species to laboratory rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science: JAALAS, 50*, 926.

Lutz, C. K., Coleman, K., Worlein, J., & Novak, M. A. (2013). Hair loss and hair-pulling in rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science: JAALAS, 52,* 454-457.

Lutz, C. K., & Farrow, R. A. (1996). Foraging device for singly housed longtailed macaques does not reduce stereotypies. *Contemporary Topics, 35,* 75 – 78.

Lutz, C. K., & Novak, M. A. (2005). Environmental enrichment for nonhuman primates: Theory and application. *ILAR journal / Institute of Laboratory Animal Resources, 46*, 178-191.

Lutz, C. K., & Sharp, R. M. (2015). Alopecia in outdoor group- and corral-housed baboons (*Papio hamadryas spp.*). *Journal of the American Association for Laboratory Animal Science, 54,* 384-388.

Lutz, C. K., Well, A., & Novak, M. A. (2003). Stereotypic and self-injurious behavior in rhesus macaques: A survey and retrospective analysis of environment and early experience. *American Journal of Primatology, 60*, 1-15. doi: 10.1002/ajp.10075

Macy, J. D., Jr., Beattie, T. A., Morganstern, S. E., & Arnstern, A. F. (2000). Use of guanfacine to control self-injurious behavior in two rhesus macaques (*Macaca mulatta*) and one baboon (*Papio anubis*). *Comparative Medicine, 50,* 419 – 425.

Major, C. A., Kelly, B. J., Novak, M. A., Davenport, M. D., Stonemetz, K. M., & Meyer, J. S. (2009). The anxiogenic drug FG7142 increases self-injurious behavior in male rhesus monkeys (*Macaca mulatta*). *Life Sciences, 85*, 753-758.

Marinus, L., Chase, W., Rasmussen, K., Jorgensen, M., & Novak, M. A. (1999). Reaction of rhesus monkeys with self-injurious behavior to heart rate testing: Is biting a coping strategy. *American Journal of Primatology, 49,* 79.

Martin, A. L. (2015). The primatologist as a behavioral engineer. *American Journal of Primatology*. Advance online publication. doi: DOI: 10.1002/ajp.22500

Martin, A. L., Bloomsmith, M. A., Kelley, M. E., Marr, M. J., & Maple, T. L. (2011). Functional analysis and treatment of human-directed undesirable behavior exhibited by a captive chimpanzee. *Journal of Applied Behavior Analysis, 44,* 139 – 143.

Martin, A. L., Perlman, J. E., & Bloomsmith, M. A. (2011). Evaluating the relationship between hair loss and behavior in captive nonhuman primates. [Abstract]. *American Journal of Primatology, 73(S1)*, 107.

Mason, G. (1991a). Stereotypies and suffering. *Behavioural Processes, 25,* 103-115.

Mason, G. (1991b). Stereotypies: A critical review. *Animal Behaviour, 41*, 1015-1037.

Mason, G., & Latham, N. R. (2004). Can't stop, won't stop: Is stereotypy a reliable animal welfare indicator? *Animal Welfare, 13(Suppl 1),* 57-69.

Meyer, J. S., Novak, M. A., Bowman, R. E., & Harlow, H. F. (1975). Behavioral and hormonal effects of attachment object separation in surrogate-peer-reared and mother-reared infant rhesus monkeys. *Developmental Psychobiology, 8*, 425-435. doi: 10.1002/dev.420080507

Midi, H., Sarkar, S. K., & Rana, S. (2010). Collinearity diagnostics of binary logistic regression model. *Journal of Interdisciplinary Mathematics, 13*, 253-267.

Miltenberger, R. G. (2005). The role of automatic negative reinforcement in clinical problems. *International Journal of Behavioral Consultation and Therapy, 1,* 1-11.

Mitchell, G. D., Raymond, E., Ruppenthal, G., & Harlow, H. (1966). Long-term effects of total social isolation upon behavior of rhesus monkeys. *Psychological Reports, 18*, 567-580.

National Research Council of the National Academies. (2011). *Guide for the care and use of laboratory animals. Eighth edition*. Washington, DC: The National Academies Press.

National Research Council. (1998). *The psychological well-being of nonhuman primates*. Washington, DC: National Academy Press.

Novak, M. A. (2003). Self-injurious behavior in rhesus monkeys: New insights into its etiology, physiology, and treatment. *American Journal of Primatology, 59*, 3-19.

Novak, M. A., Hamel, A. F., Coleman, K., Lutz, C. K., Worlein, J., Menard, M., . . . Meyer, J. S. (2014). Hair loss and hypothalamic–pituitary–adrenocortical axis activity in captive rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science, 53*, 261-266.

Novak, M. A., Kelly, B. J., Bayne, K., & Meyer, J. S. (2012). Behavioral disorders of nonhuman primates. In C. R. Abee, K. Mansfield, S. Tardif & T. Morris (Eds.), *Nonhuman Primates in Biomedical Research: Biology and Management* (Vol. 1, pp. 177 - 196). Waltham, MA: Elsevier.

Novak, M. A., Kinsey, J. H., Jorgensen, M. J., & Hazen, T. J. (1998). Effects of puzzle feeders on pathological behavior in individually housed rhesus monkeys. *American Journal of Primatology, 46*(3), 213-227. doi: 10.1002/(sici)1098-2345(1998)46:3<213::aid-ajp3>3.0.co;2-l

Novak, M. A., & Meyer, J. S. (2009). Alopecia: possible causes and treatments, particularly in captive nonhuman primates. *Comparative Medicine, 59*, 18 - 26.

Novak, M. A., Meyer, J., Lutz, C. K., & Tiefenbacher, S. (2006). Deprived environments: Developmental insights from primatology. In G. Mason & J. Rushen (Eds.), *Stereotypic animal behaviour: Fundamentals and applications to welfare* (pp. 153-162). Oxfordshire: CABI.

O'Rourke, N., & Hatcher, L. (2013). *A step-by-step approach to using SAS for factor analysis and structural equation modeling* (2nd ed.). Cary, N.C.: SAS Institute Inc.

Pearson, K. (1990). Mathematical contributions to the theory of evolution. VII. On the correlation of characters not quantitatively measureable. *Philosophical Transactions of the Royal Society of London. Series A, Containing Papers of a Mathematical or Physical Character, 195*, 1- 47. Retrieved from: http://www.jstor.org/stable/90764

Reinhardt, V. (1999). Pair-housing overcomes self-biting in macaques. *Laboratory Primate Newsletter, 38(1),* 4.

Reinhardt, V. & Rossell, M. (2001). Self-biting in caged macaques: case, effect, and treatment. *Journal of Applied Animal Welfare Science, 4,* 285 – 294.

Rommeck, I., Anderson, K., Heagerty, A., Cameron, A., & McCowan, B. (2009). Risk factors and remediation of self-injurious and self-abuse behavior in rhesus macaques. *Journal of Applied Animal Welfare Science, 12*(1)*,* 61-72. doi: 10.1080/10888700802536798

Ross, S. R. & Bloomsmith, M. (2001). A comment on Birkett and Newton-Fisher (2011). *PLos One*, doi: 10.1371/journal.pone.0020101.

Runeson, E. P., Lee, G. H., Crockett, C. M., & Bellanca, R. U. (2011). Evaluating paint rollers as an intervention for alopecia in monkeys in the laboratory (*Macaca nemestrina*). *Journal of Applied Animal Welfare Science, 14*, 138-149.

Schapiro, S. J., & Bloomsmith, M. A. (1995). Behavioral effects of enrichment on singly-housed, yearling rhesus monkeys: An analysis including three enrichment conditions and a control group. *American Journal of Primatology, 35*(2), 89-101. doi: 10.1002/ajp.1350350202

Schapiro, S. J., Bloomsmith, M. A., Porter, L. M., & Suarez, S. A. (1996). Enrichment effects on rhesus monkeys successively housed singly, in pairs, and in groups. *Applied Animal Behaviour Science, 48*, 159-171. doi: 10.1016/0168-1591(96)01038-6

Schapiro, S. J., Bloomsmith, M. A., Suarez, S. A., & Porter, L. M. (1996). Effects of social and inanimate enrichment on the behavior of yearling rhesus monkeys. *American journal of primatology, 40*, 247-260. doi: 10.1002/(sici)1098-2345(1996)40:3<247::aid-ajp3>3.0.co;2-y

Soussignan, R., & Koch, P. (1985). Rhythmical stereotypies (leg-swinging) associated with reductions in heart-rate in normal school children. *Biological Psychology, 21*, 161-167.

Spring, S. E., Clifford, J. O., & Tomkol, D. L. (1997). Effect of environmental enrichment devices on behaviors of single-and group-housed squirrel monkeys (*Saimiri sciureus*). *Journal of the American Association for Laboratory Animal Science, 36*(3), 72-75.

Steinmetz, H. W., Kaumanns, W., Dix, I., Heistermann, M., Fox, M., & Kaup, F. J. (2006). Coat condition, housing condition and measurement of faecal cortisol metabolites–a non-invasive study about alopecia in captive rhesus macaques (*Macaca mulatta*). *Journal of Medical Primatology, 35*, 3-11.

Steinmetz, H. W., Kaumanns, W., Dix, I., Neimeier, K. A., & Kaup, F. J. (2005). Dermatologic investigation of alopecia in rhesus macaques (Macaca mulatta). *Journal of Zoo and Wildlife Medicine, 36,* 229 – 238. doi: http://dx.doi.org/10.1638/04-054.1

Tarou, L. R., Bloomsmith, M. A., & Maple, T. L. (2005). Survey of stereotypic behavior in prosimians. *American Journal of Primatology, 65*, 181-196. doi: 10.1002/ajp.20107

Tiefenbacher, S., Fahey, M. A., Rowlett, J. K., Meyer, J. S., Pouliot, A. L., Jones, B. M., & Novak, M. A. (2005). The efficacy of diazepam treatment for the management of acute wounding episodes in captive rhesus macaques. *Comparative Medicine, 55*, 387-392.

Tiefenbacher, S., Novak, M. A., Jorgensen, M. J., & Meyer, J. S. (2000). Physiological correlates of self-injurious behavior in captive, socially-reared rhesus monkeys. *Psychoneuroendocrinology, 25*, 799-817. doi: 10.1016/s0306-4530(00)00027-5

Tiefenbacher, S., Novak, M. A., Marinus, L. M., Chase, W. K., Miller, J. A., & Meyer, J. S. (2004). Altered hypothalamic-pituitary-adrenocortical function in rhesus monkeys (*Macaca mulatta*) with self-injurious behavior. *Psychoneuroendocrinology, 29*, 501-515.

Tully, L., Jenne, M., & Coleman, K. (2002). Paint roller and grooming boards as treatment for over-grooming rhesus macaques. *Contemporary Issues in Laboratory Animal Science, 41*, 75.

United States Department of Agriculture (USDA). (1991). *Animal welfare, standards, final Rule (Part 3 Subpart D: Specifications for the humane handling, care, treatment, and transportation of nonhuman primates)*. Fed. Reg. US. (56 FR 6495). Retrieved from United States Government Printing Office: https://www.gpo.gov/fdsys/pkg/CFR-2000-title9-vol1/pdf/CFR-2000-title9-vol1-part3-subpartD.pdf

Weed, J. L., Wagner, P. O, Byrum, R., Parrish, S., Knezevich, M., & Powell, D. A. (2003). Treatment of persistent self-injurious behavior in rhesus monkeys through socialization: a preliminary report. *Contemporary Topics, 42,* 21 – 23.

Weld, K. P., Mench, J. A., Woodward, R. A., Bolesta, M. S., Suomi, S. J., & Higley, J. D. (1998). Effect of tryptophan treatment on self-biting and central nervous system serotonin metabolism in rhesus monkeys (*Macaca mulatta*). *Neuropsychopharmacology, 19,* 314 – 321.

Yerkes, R. M. (1925). *Almost human*. New York: The Century Company.